

COSMETIC AND PERFUMERY  
RAW MATERIALS

# Manufacturing Chemist

*incorporating*  
**MANUFACTURING PERFUMER**

Vol. XXXII No. 11

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NOVEMBER 1961



RIGHT

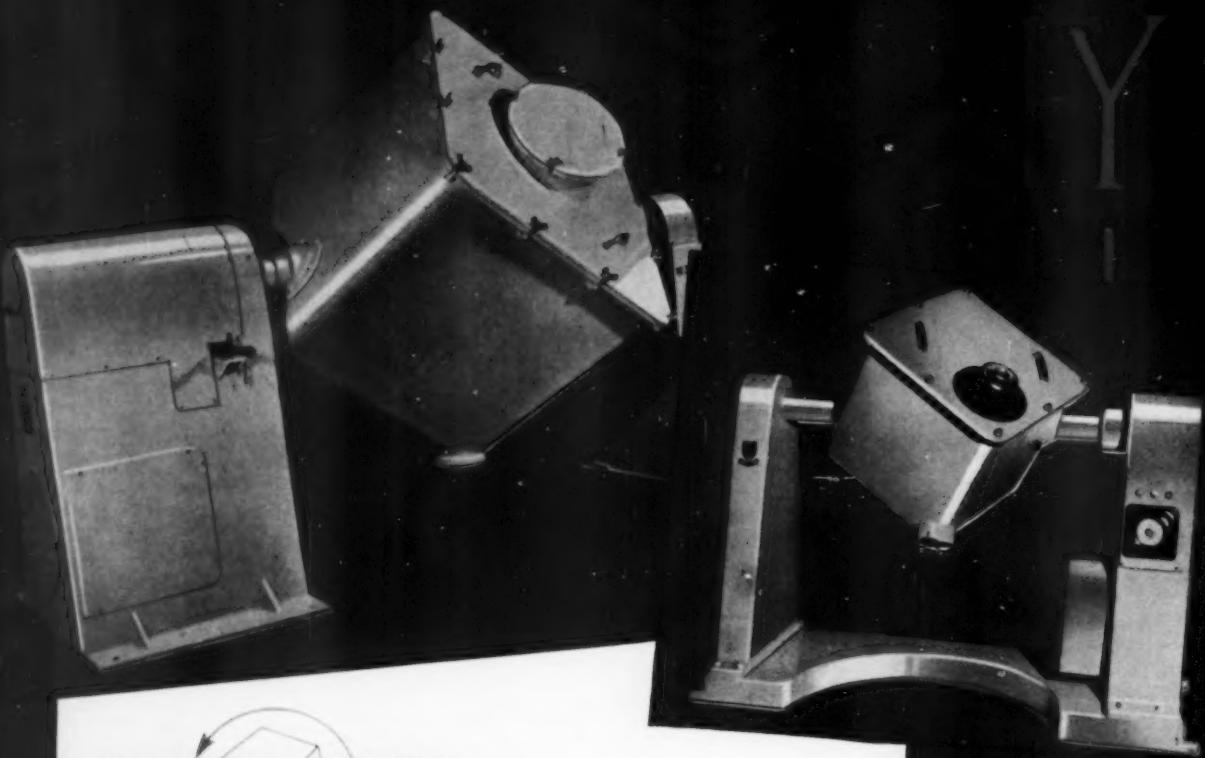
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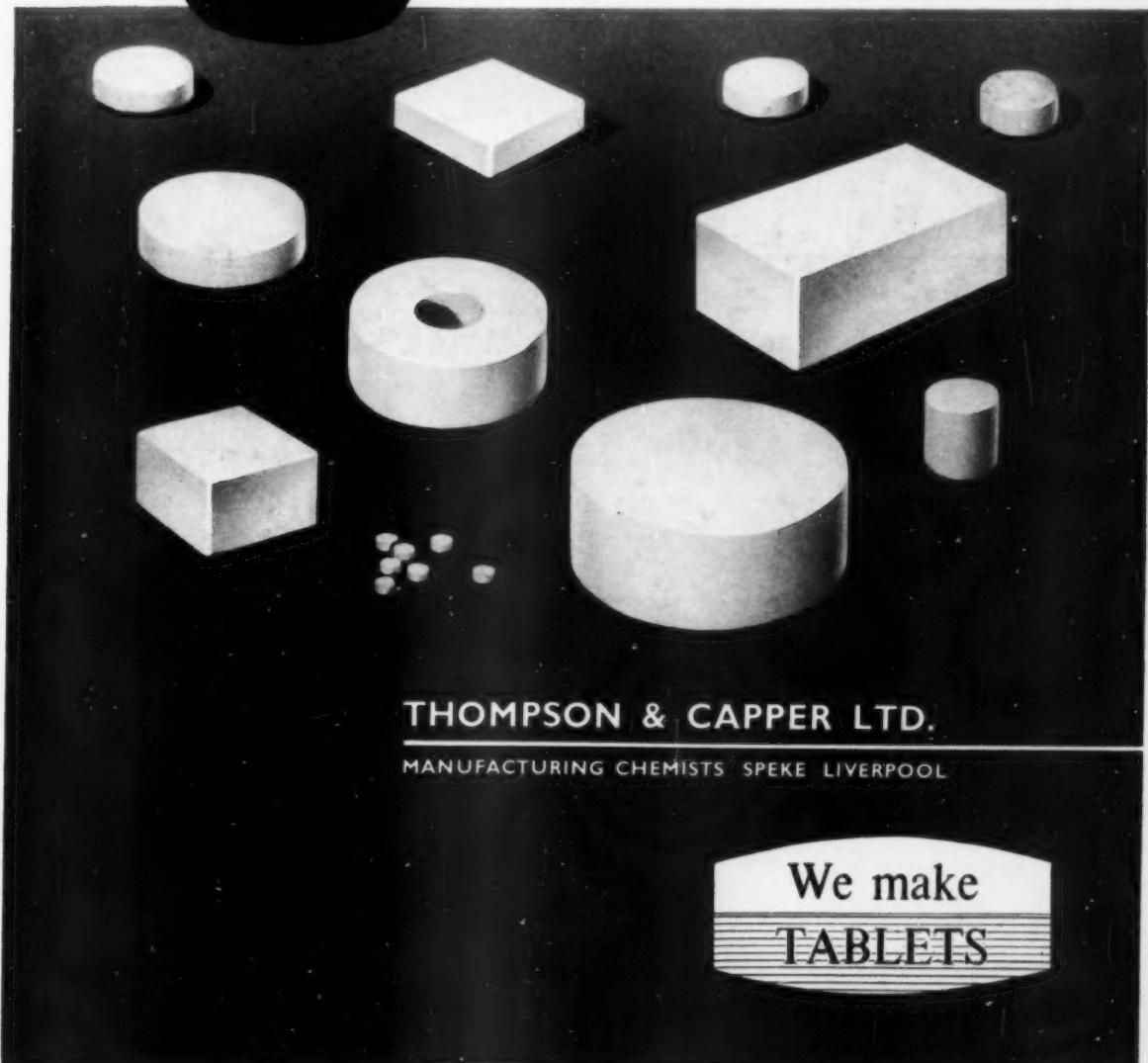
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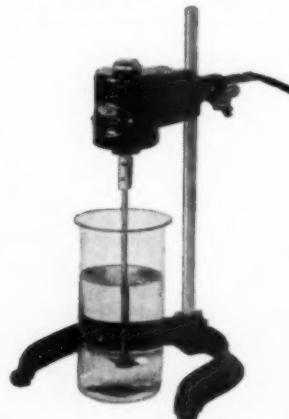
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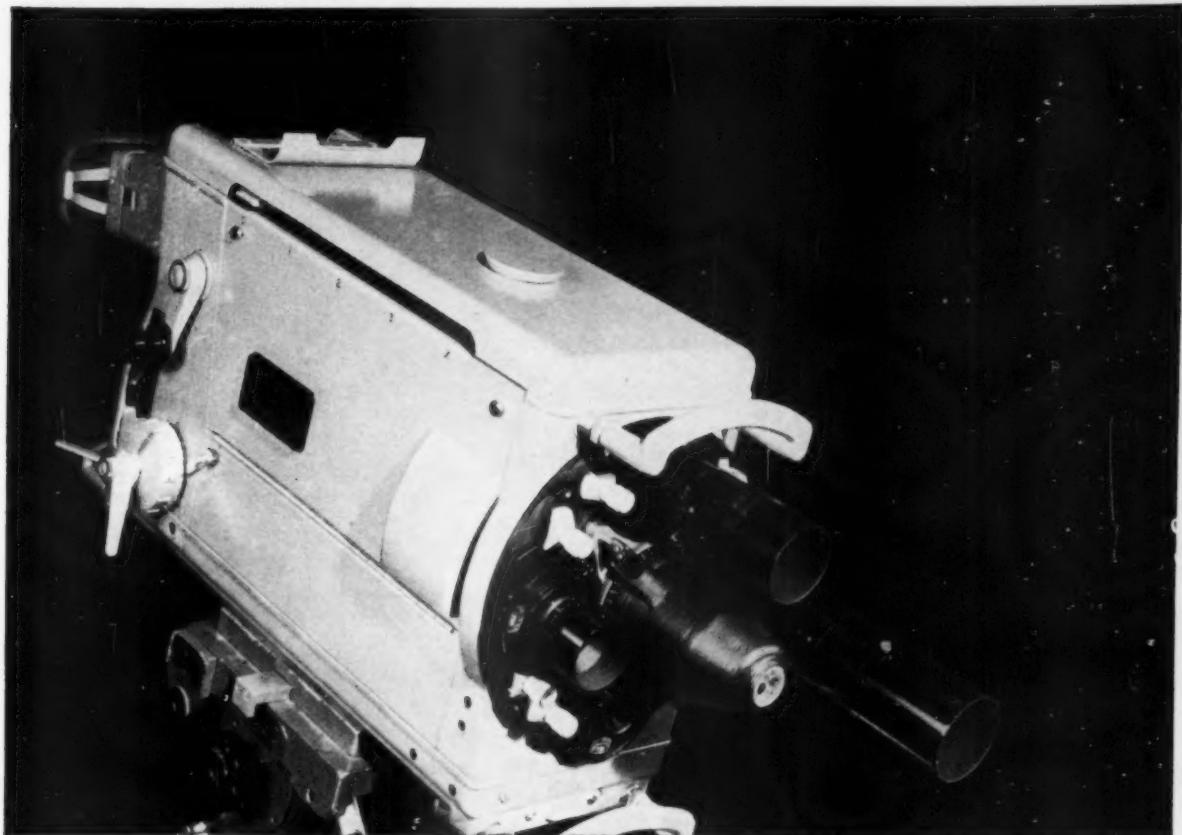
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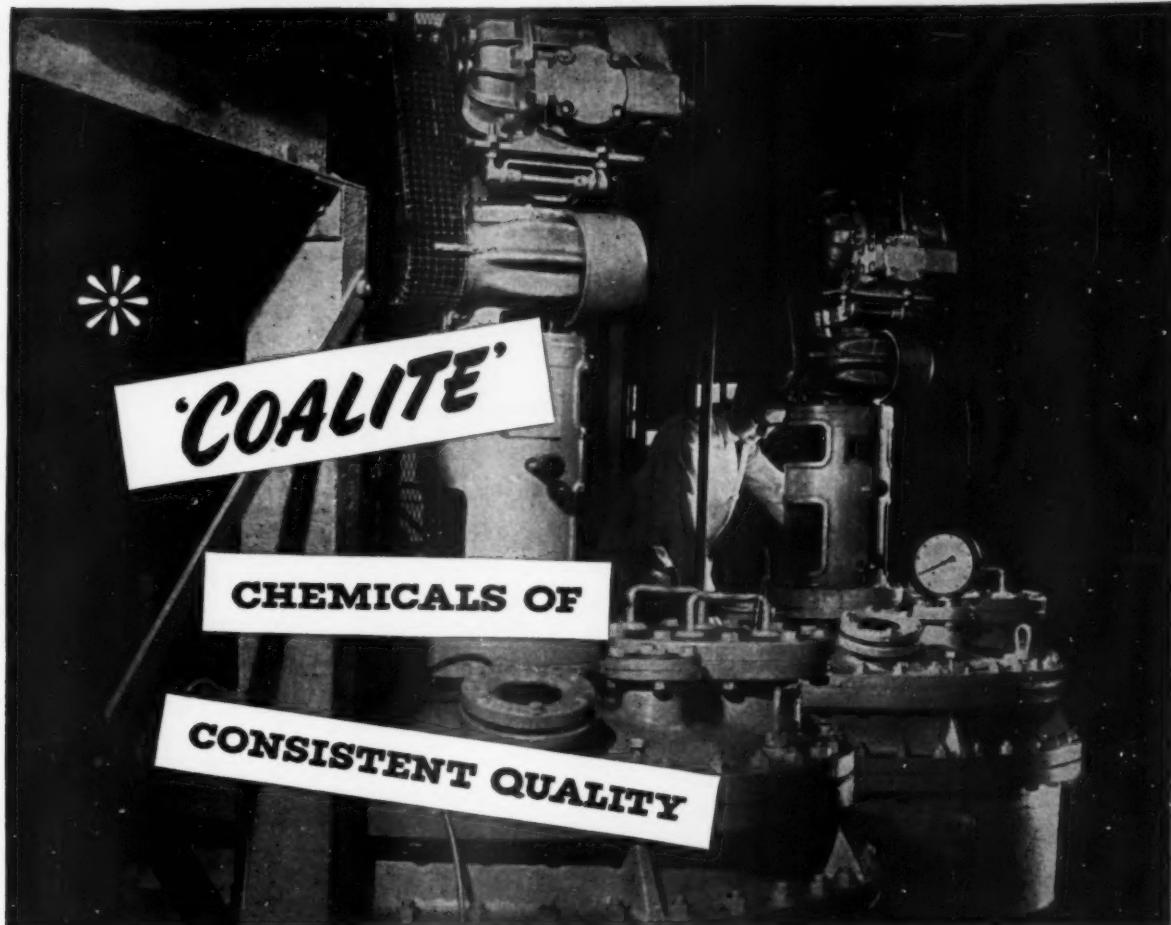
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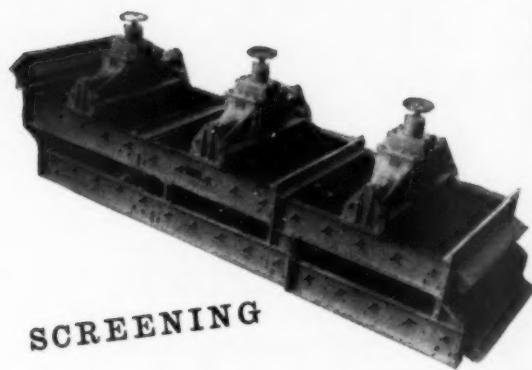
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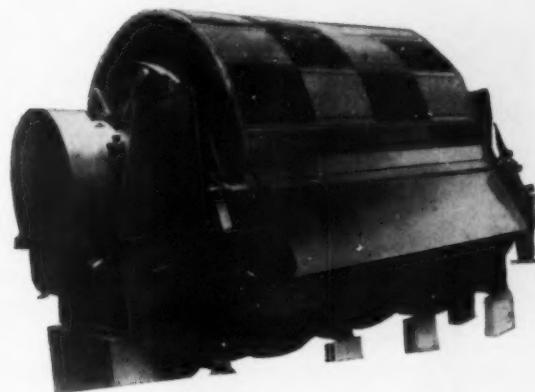
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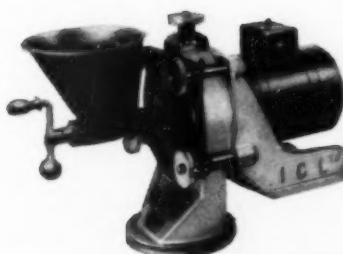
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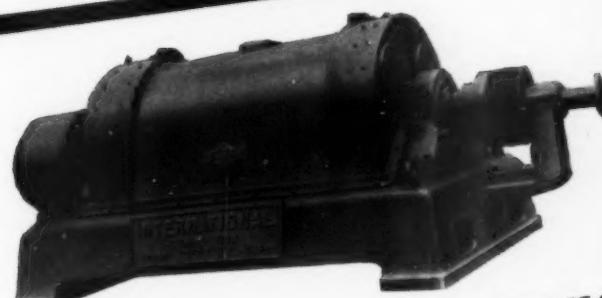
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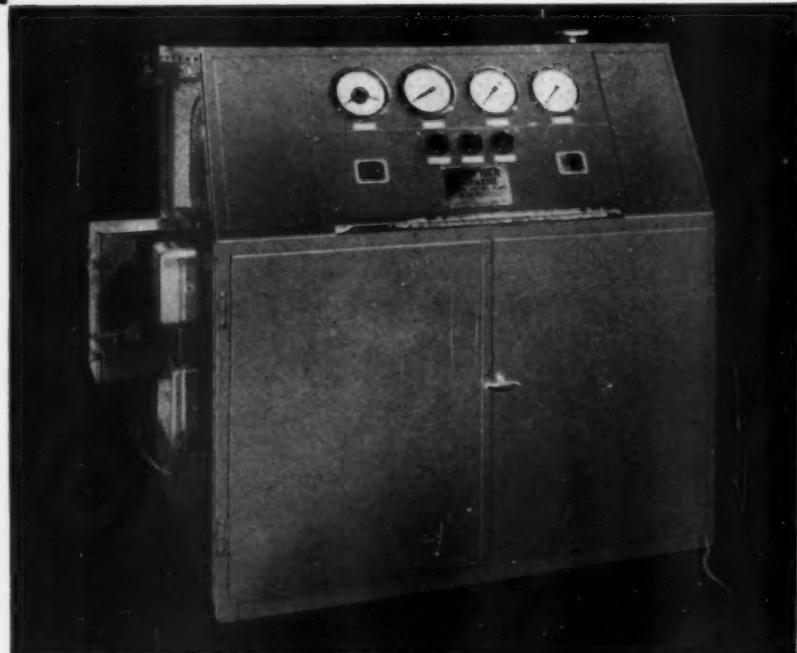
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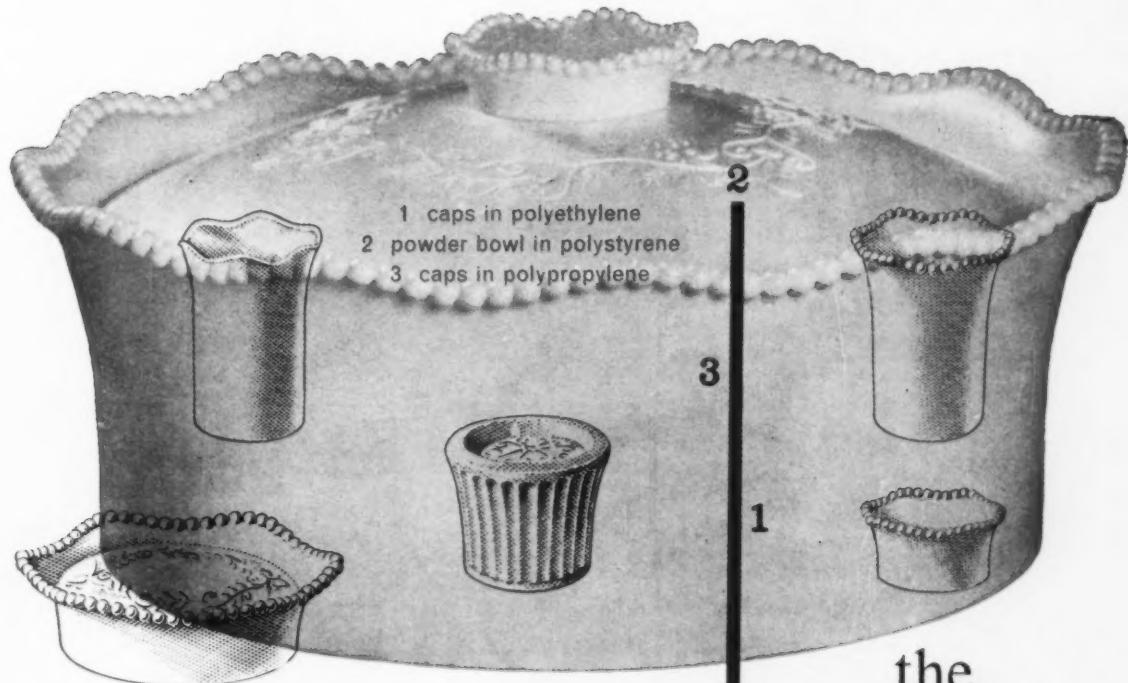
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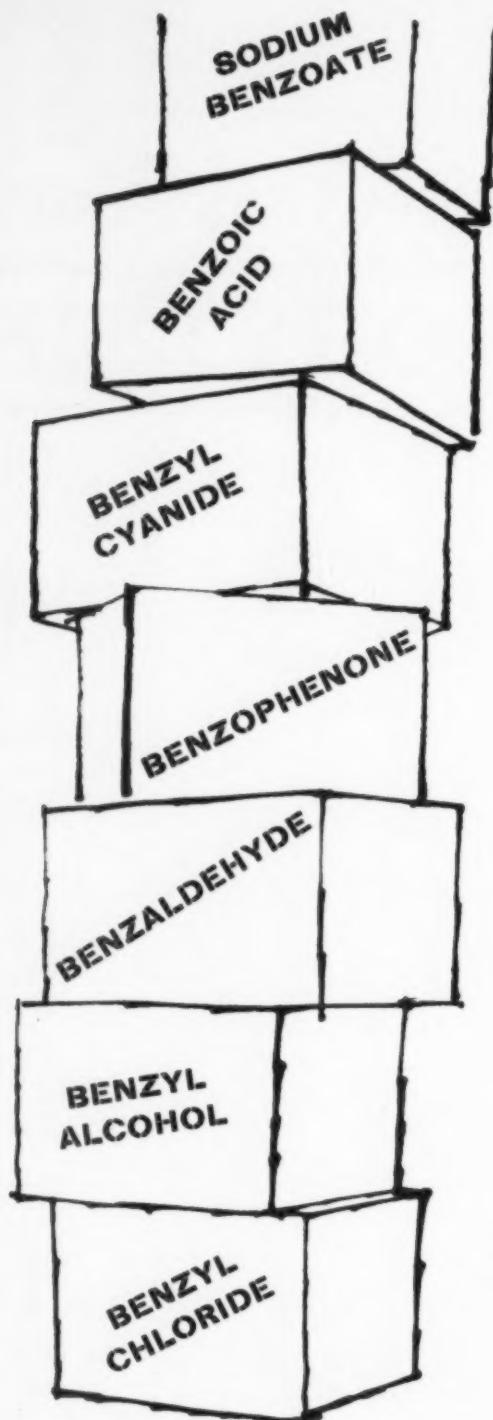
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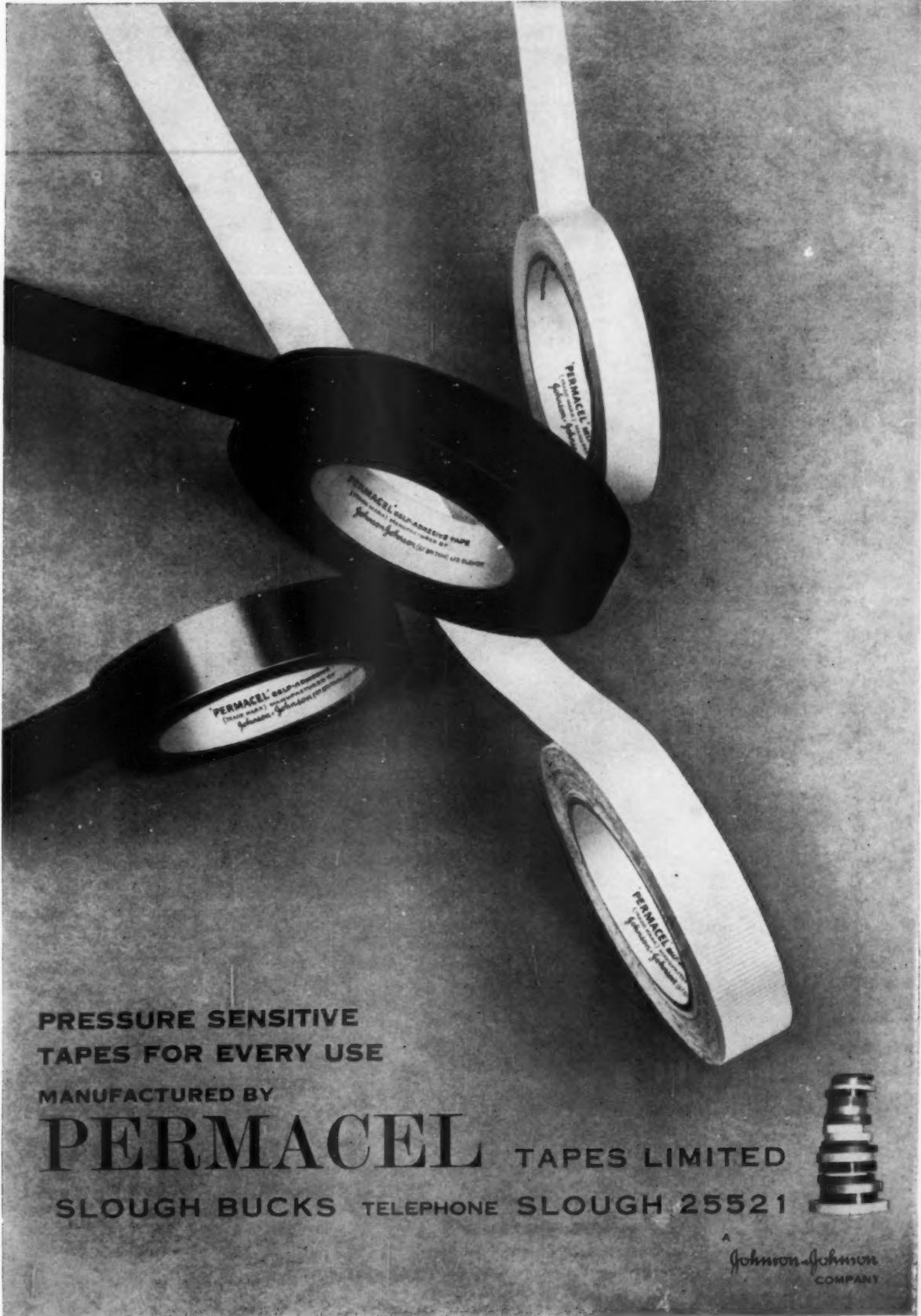
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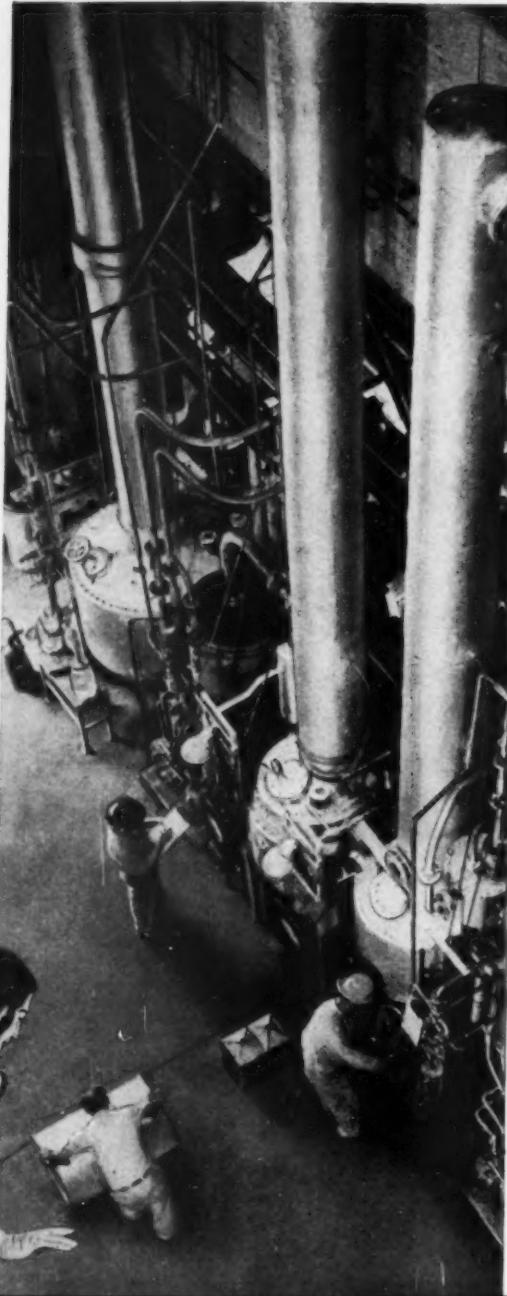


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If so, have you considered how the use of Alu-Pharm adhesive aluminium bottle capsules could be the immediate answer to your problem?

The adhesive coating ensures a perfect seal, making your product tamper-proof.

The Alu-Pharm capsules are available in a large range of colours and sizes suitable for sealing bottles whichever closure is used.

They can be applied at high speed and cost less than any other metal capsule.

*May we quote for your requirements?*

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ADHESIVE  
LABELLING  
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It's a *Tickogrip* (the label that grips and stays put).

**JUST ONE**  
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**TAKE ONE OFF**  
and press it to any firm surface—see how it sticks and sticks!

**APPLY THE OTHER TO YOUR LETTER-PAPER**  
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apply labels  
with  
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It's the fantastic new 'baby' of a  
**FULL RANGE**  
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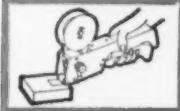
#### SEE HOW IT WORKS



**1 PRINT**  
You squeeze  
the grip—the  
ticket is  
printed.



**2 DISPENSE**  
You release  
the grip—the  
printed ticket  
is released for  
sticking on.



**3 APPLY**  
You apply the  
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object's flat  
surface and  
pull down—  
PRESTO!

NOW  
TURN  
OVER



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**Tickopy Applicators**  
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... Come along with this →

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toy

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—absolutely the first, last and *only* word for miles and miles of the best labels . . . blank or ready-printed, mirror-glazed, gold foil, silver foil, day-glo, that will stay put or will remove easily, that can replace metal plates or will stick on fabrics . . . dispensed with blissful ease from the extensive range of *Tickopoly* dispensers, applicators and overprinters.

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The Rapisonic links precision engineering and high quality emulsions. The patented liquid whistle, shown in the making, is already used by several thousand manufacturers who can vouch for the economy and efficiency of the Rapisonic. Let us help you to prepare your emulsions more quickly and cheaply - please write for full details or visit our laboratory.

Ultrasonics Ltd

Westgate Otley  
Yorkshire  
Telephone Otley 3221

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# Rapisonic

The Rapisonic links precision engineering and high quality emulsions. The patented liquid whistle, shown in the making, is already used by several thousand manufacturers who can vouch for the economy and efficiency of the Rapisonic.

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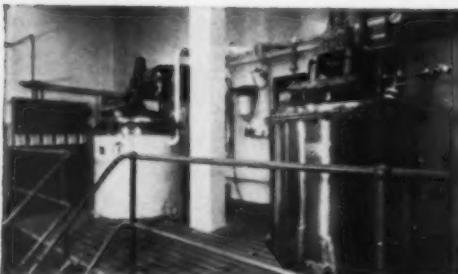
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# Giusti built better built



A 200 gallon steam-jacketed pan with 4 speed counter-rotating agitator.  
Photo by kind permission of Helena Rubinstein Limited.



Manufacturing Chemists' Process Plant.  
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TOTE containers, metal  
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economical way to store  
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In handling efficiency  
they are unequalled. In  
the safety of tote bins  
there is no loss of material  
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# TOTE SYSTEM

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## TOTE BINS

Aluminium, mild or stainless steel Tote Bins are available in standard capacities of 42, 74, 95 and 110 cu ft.

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One or more Tote Tilt Discharge Units, depending on your plant layout and process requirements.

LET US DO A SITE SURVEY FOR YOU

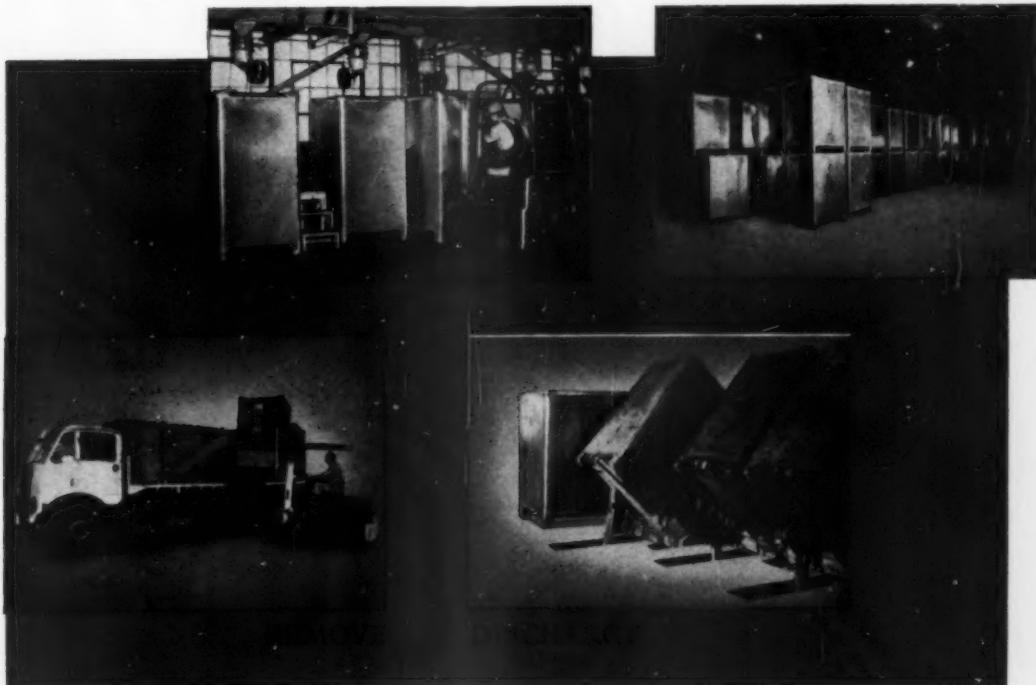
We will be glad to undertake a Site Survey and assess for you the economies possible within your existing plant layout.

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We operate comprehensive hire schemes to cover all Tote equipment—Bins, Tilt Discharge Units, Weigh Scales, Level Controls and other Ancillary Equipment.

**TOTE SYSTEM** will quickly, easily and economically solve your bulk handling problems, and rapidly **PAY FOR ITSELF** by—

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- 5** Reducing labour and handling costs.
- 6** Preserving original product quality.
- 7** Speeding up vehicle turn-round.



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China Clay  
Cornflour  
Custard Powder  
Diathene  
Flour  
Frit  
Glass Batch  
Ground Rice  
Instant Coffee  
Lacquer  
Melamine Moulding Powder  
Milk Powder  
Oil Additives  
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Phenolic Resins  
Pitch Granules  
Plastisol P.V.C.  
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Polyethylene Chips  
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Polystyrene  
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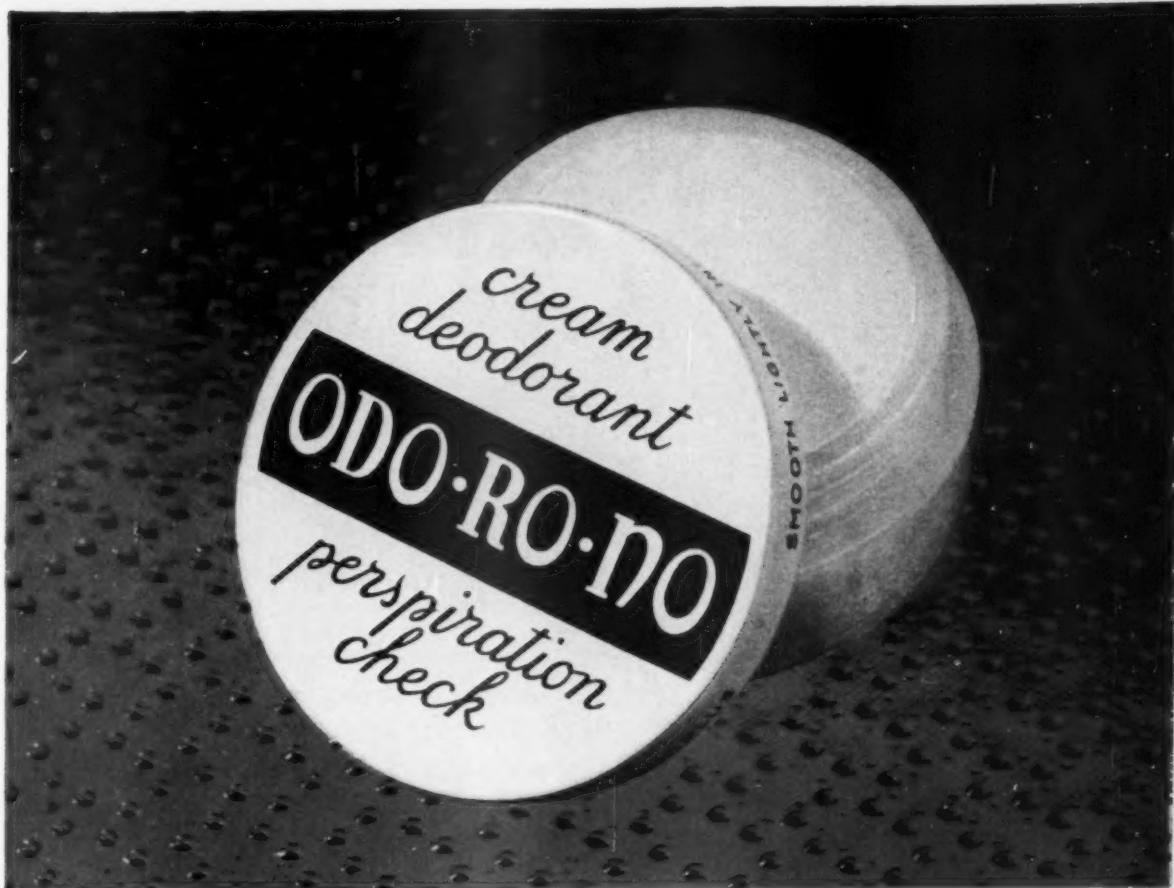
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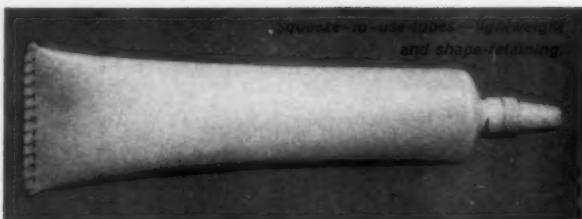
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Armoured bottles that need no outer packing—5 gal. & 10 gal.



**POLYTHENE TUBES**  
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**BAGS**  
**ARMOURED BOTTLES**

# UNBREAKABLE Cascelloid CONTAINERS

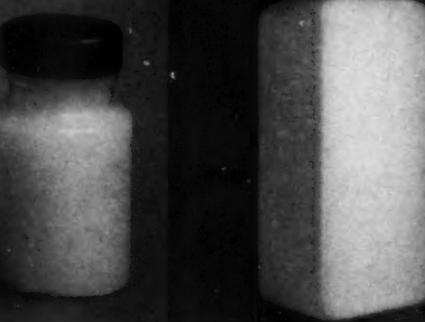


Cascelloid ranges of polythene tubes, bottles, packs and other specialised containers may well provide the perfect solution to your packaging problems. Wealth of experience and scale of production enable Cascelloid containers—lightweight and virtually indestructible—to be offered in great variety at realistic prices. They are suitable for almost any type of contents.

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for the fastest knock-down

- 25% by weight of total pyrethrins
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BEATSON, CLARK & CO. LTD.

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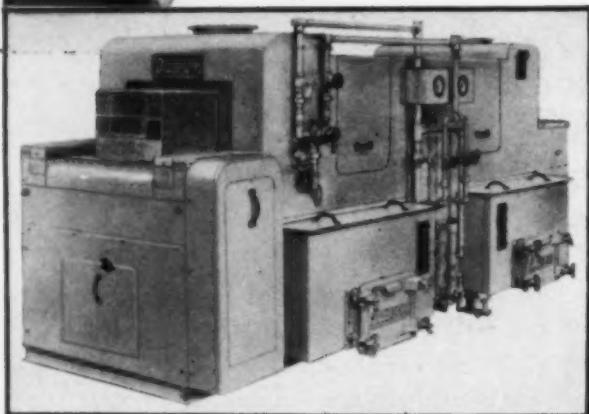
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*Done  
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No, not by a long stretch yet!

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*Whatever your  
cleaning problems  
it will pay you to  
consult Dawsons.*

Dawson

## *Animal-Cage Cleaning Machines*

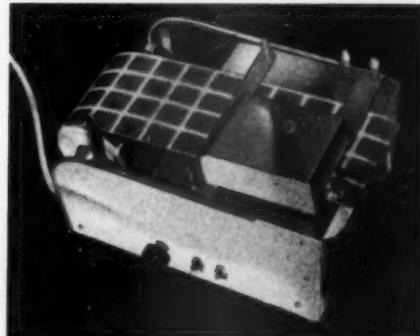
**Dawson Bros. Ltd., Gomersal, near Leeds.**

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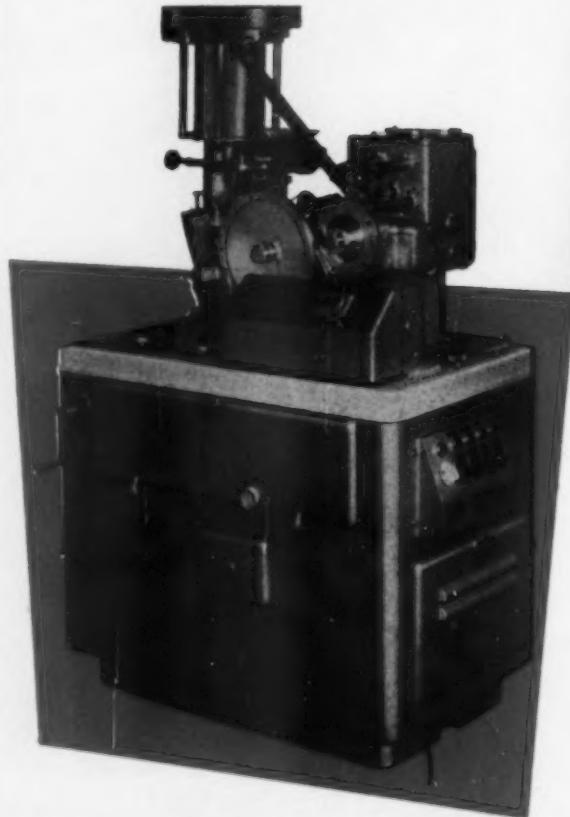
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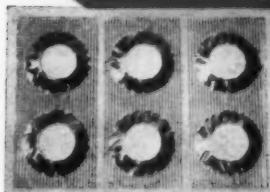
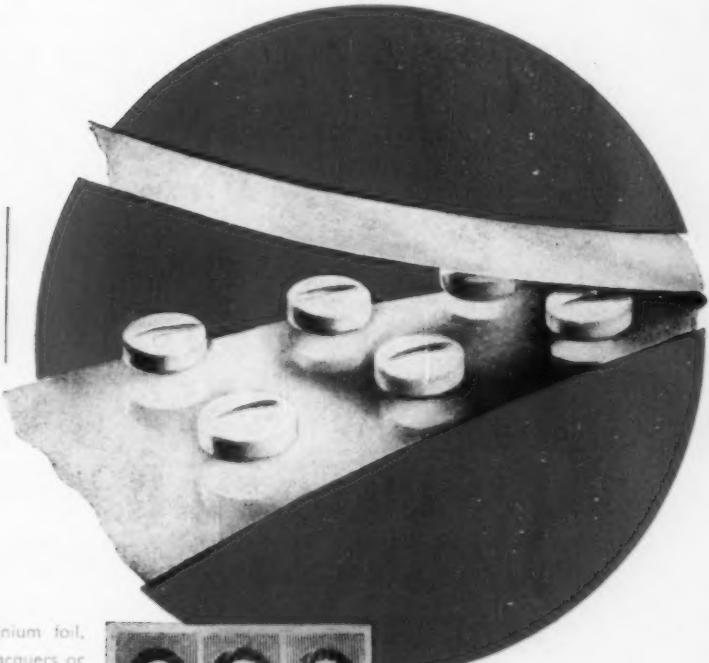
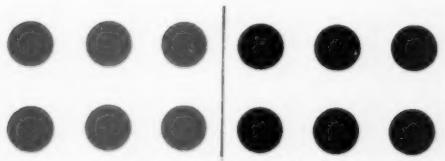
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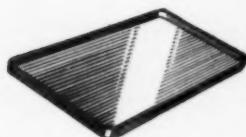
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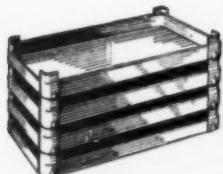
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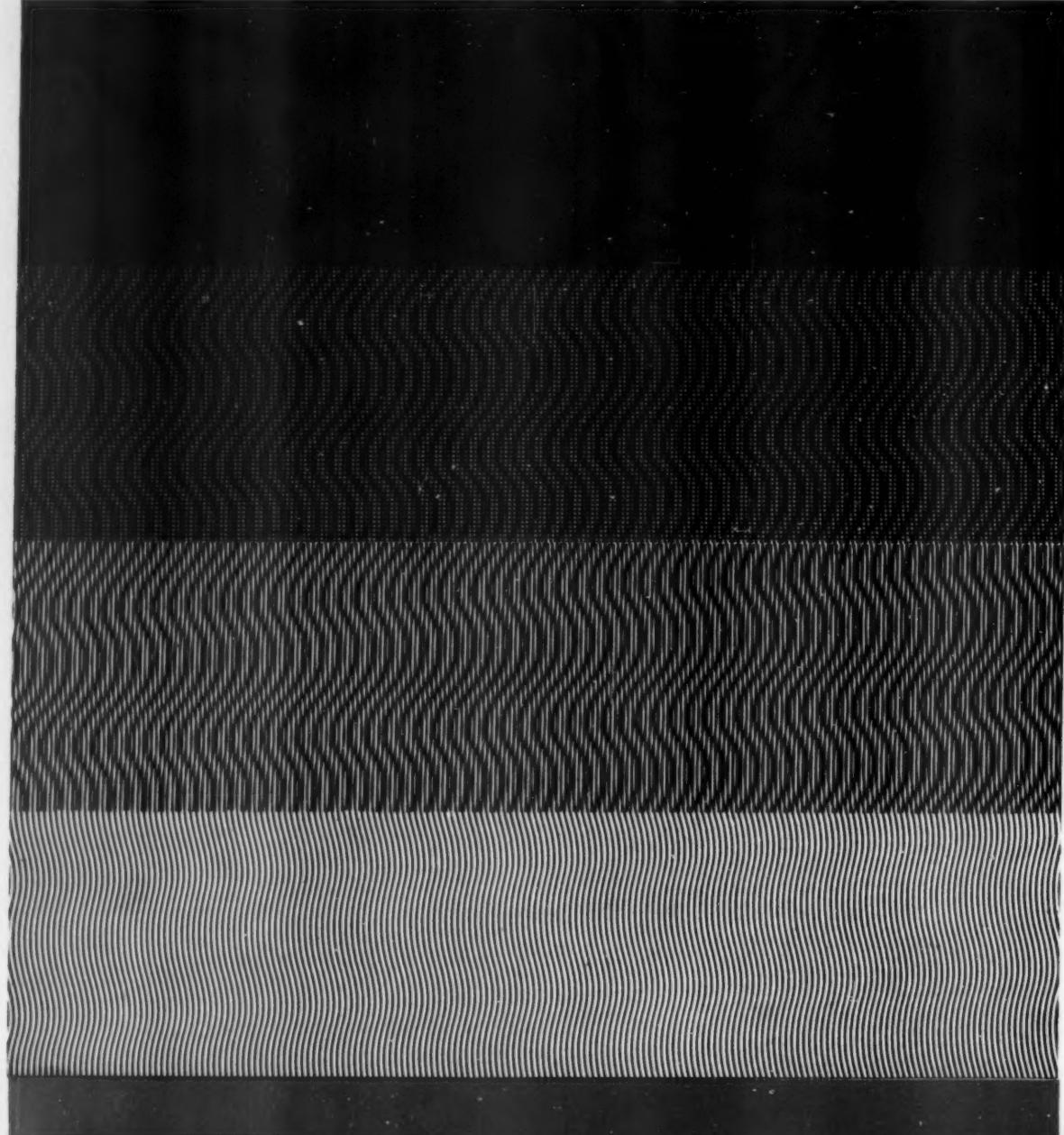


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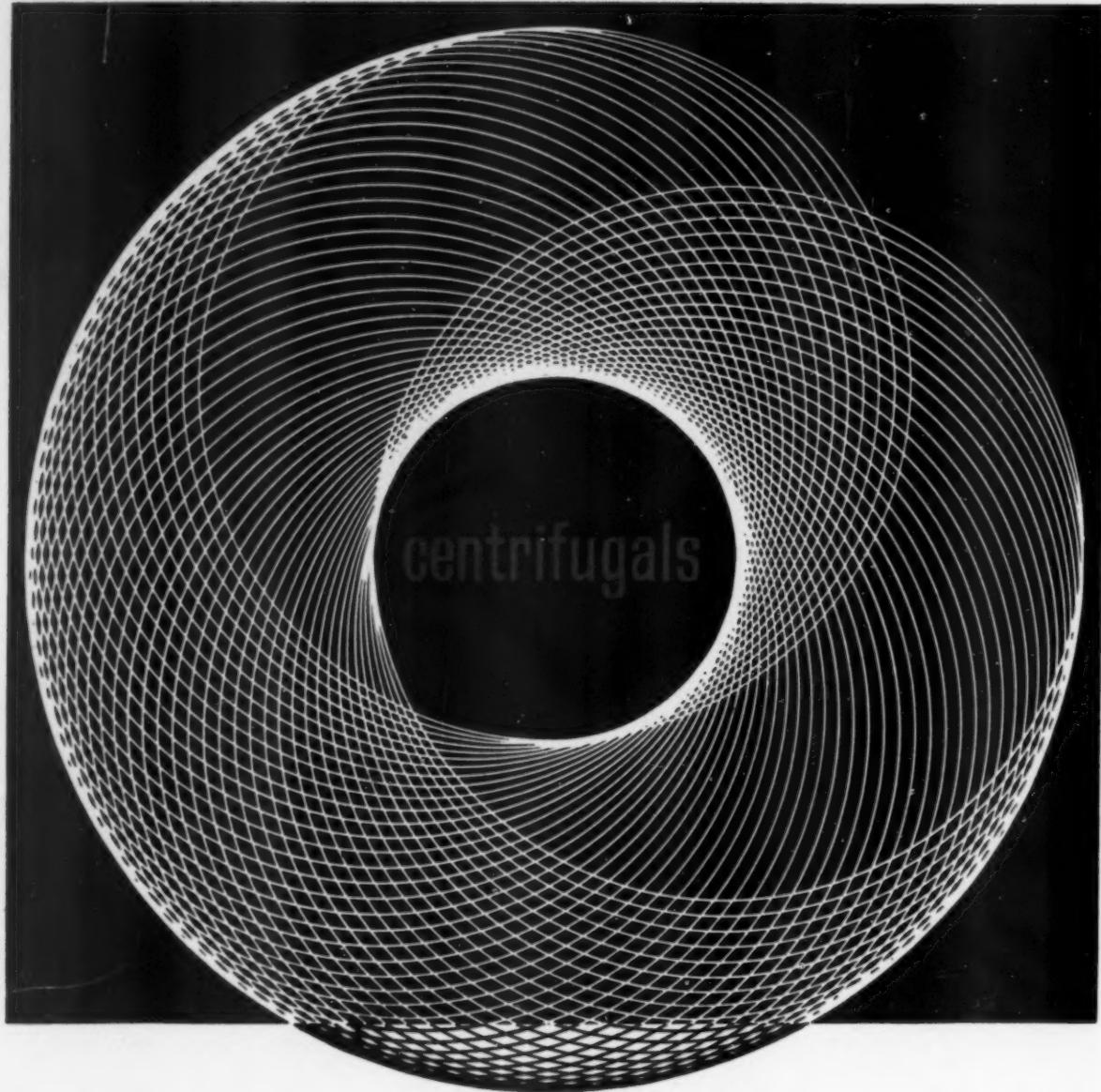


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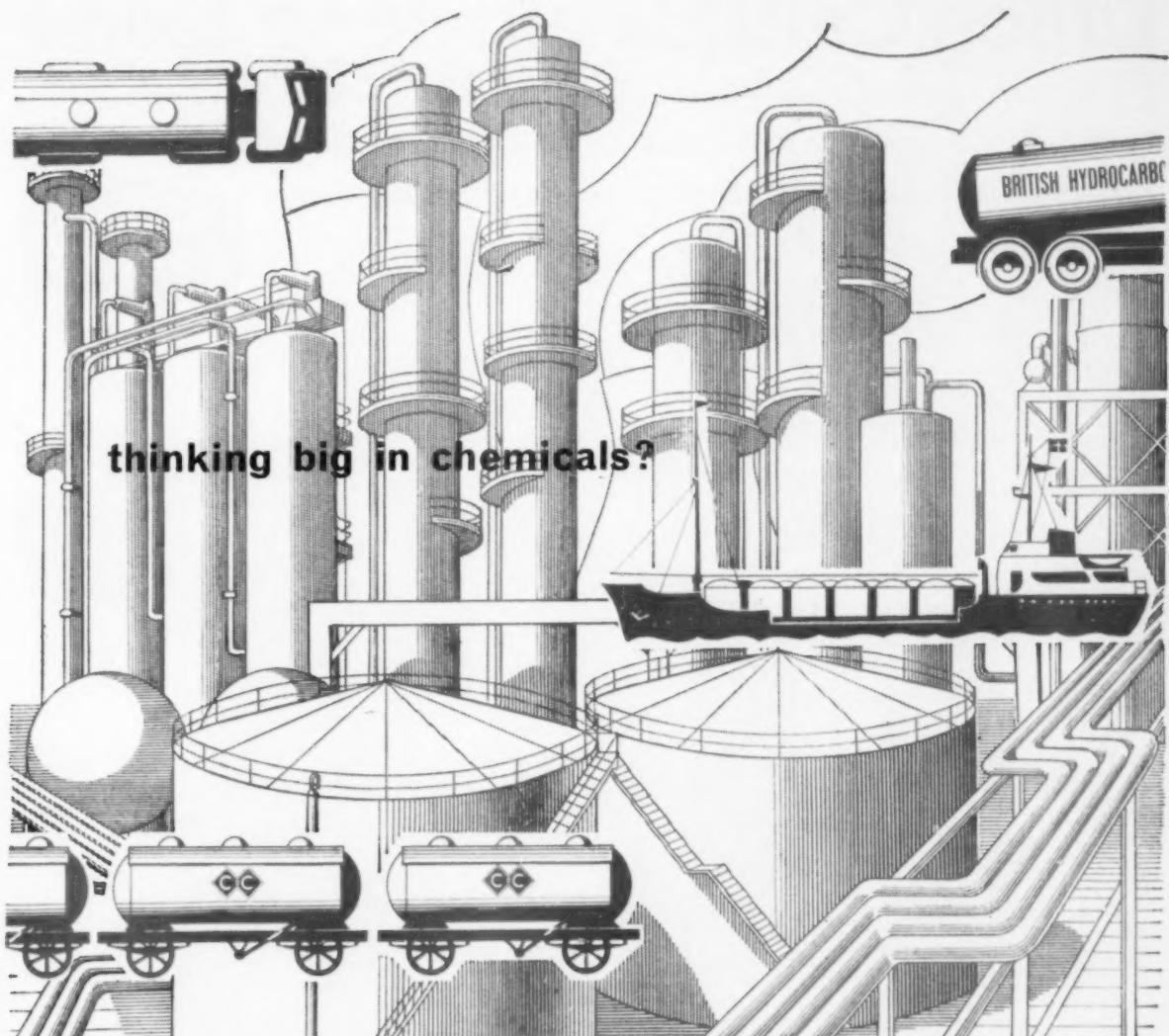
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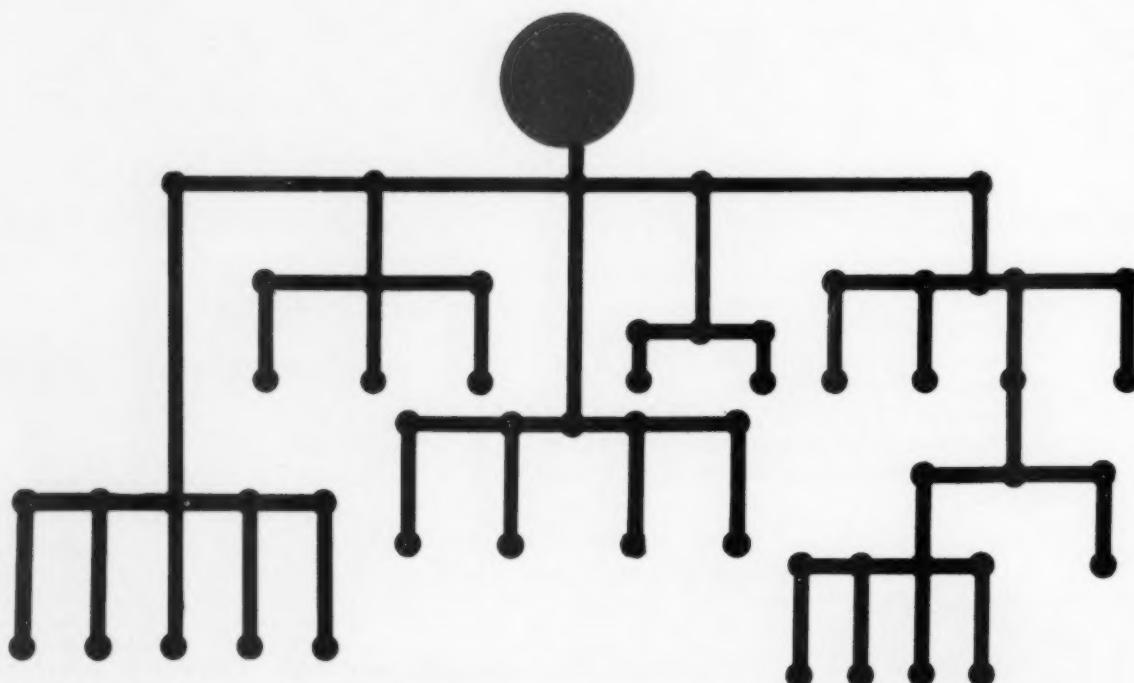
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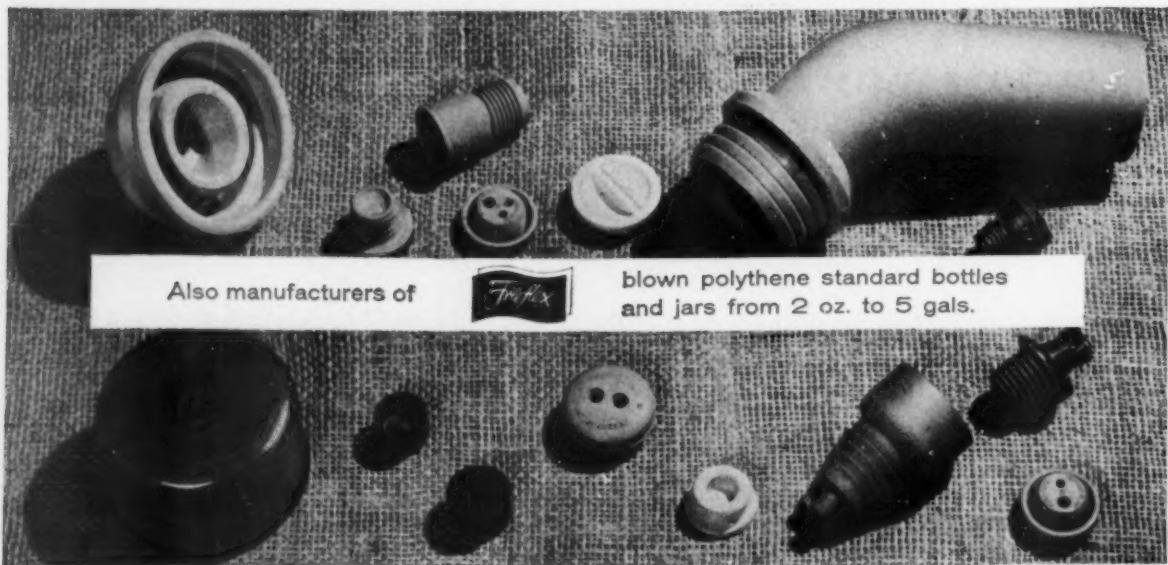


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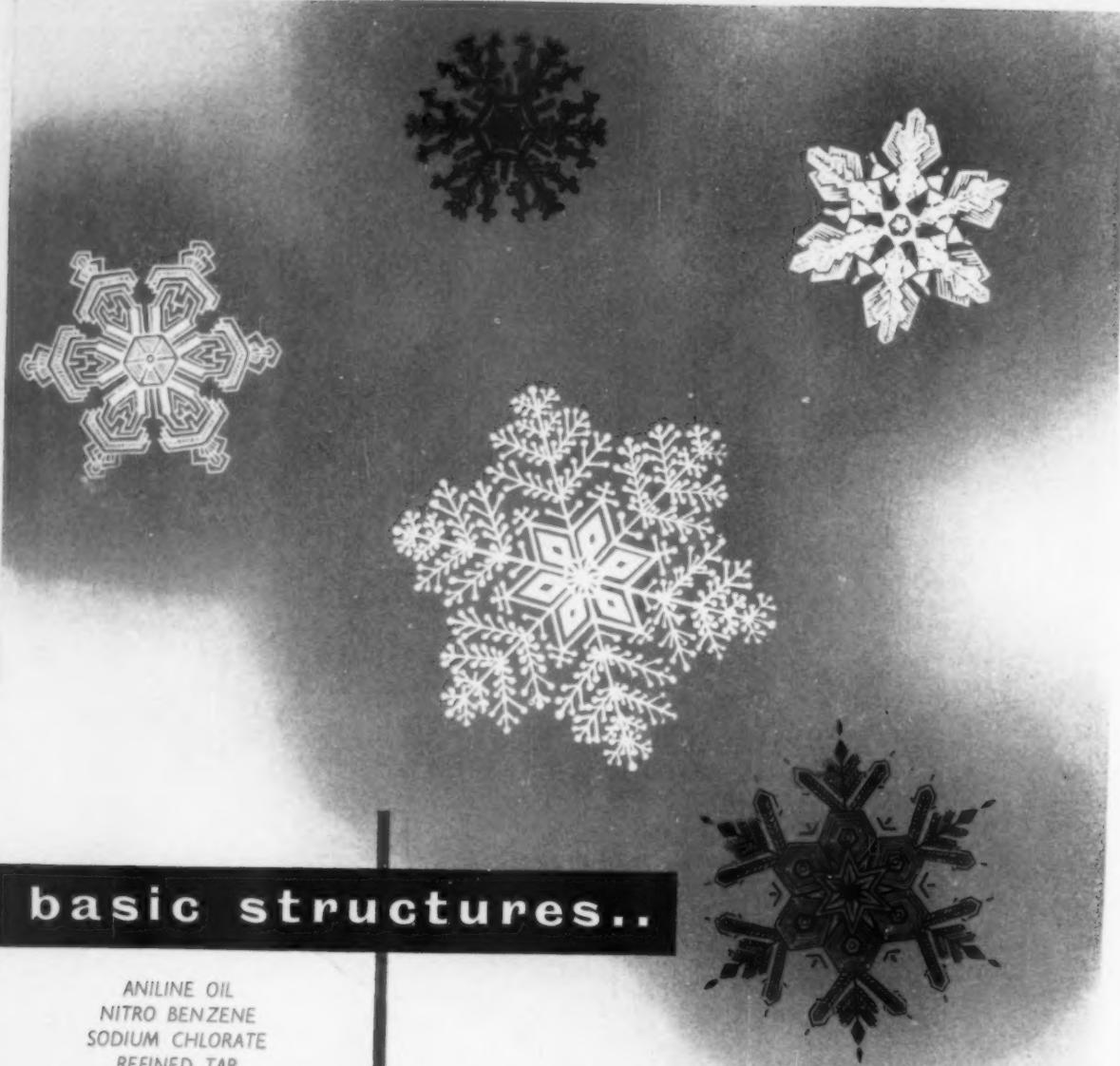
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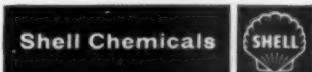
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90/16

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The design and colour of your unit packs on the wholesale and retail shelves speak for themselves when wrapped in transparent DIOphane cellulose film, which adds a quality appearance and sales appeal.

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For fuller information on this practical and economical method of wrapping consult . . .

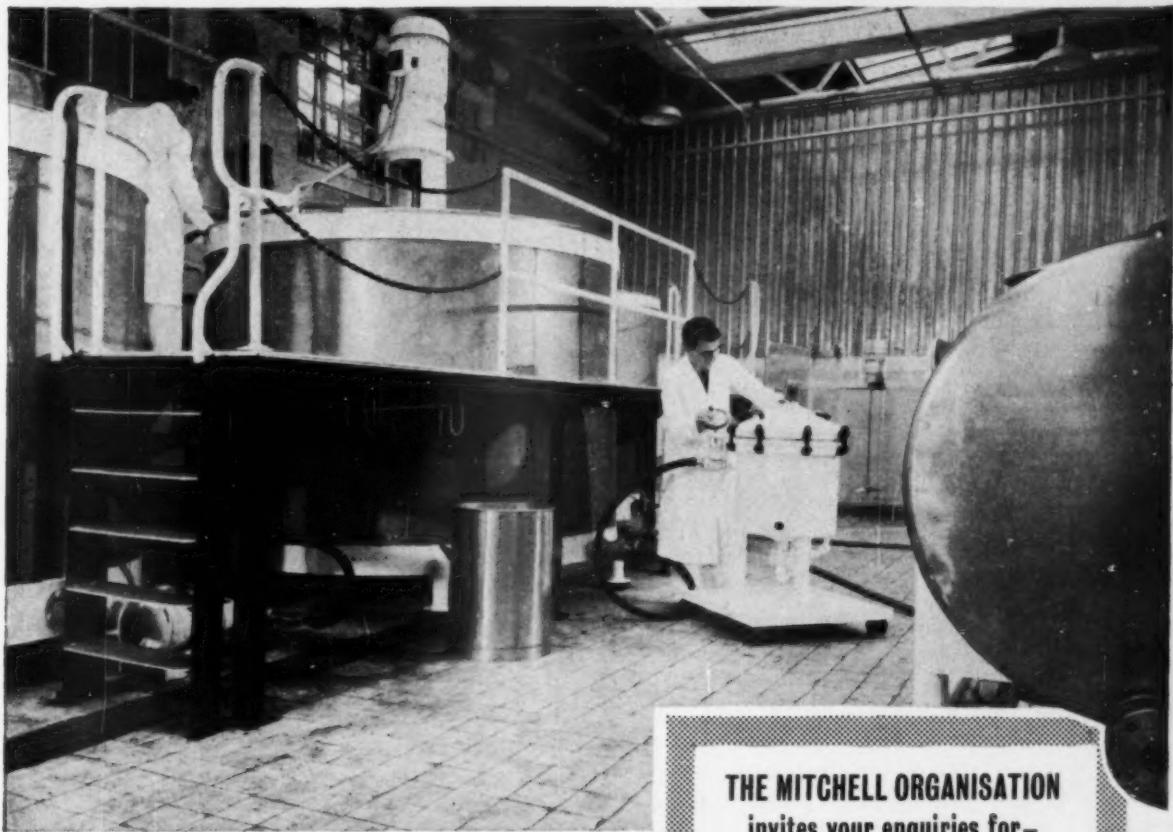
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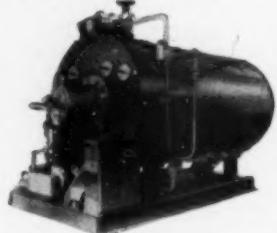


Fisons Fertilizers Ltd. just one of the many well-known organisations with Powermaster installations, utilise the great flexibility of Powermaster oil-fired packaged boilers in their new liquid ammonium nitrate factory. Every few weeks there is a peak demand for 30,000lb/hr. of steam to start a 2,500kW turbine driving a turbo-compressor, the main unit of the nitric acid plant. A battery of Model 500 Powermaster boilers meets this need, these being found more economical than electric power for this particular purpose. During normal operation the installation supplies steam for process purposes up to 10,000lb/hr.

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GWB Powermaster Model 500 has a capacity of 17,250lb/hr. of steam.



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# did Rabelais say

*"Nothing is so valuable  
as precious time"?*



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*What Rabelais actually wrote was:*

*"Rein si cher ne precieux est que le temp"*



# Seamless

## Gelatine Capsules

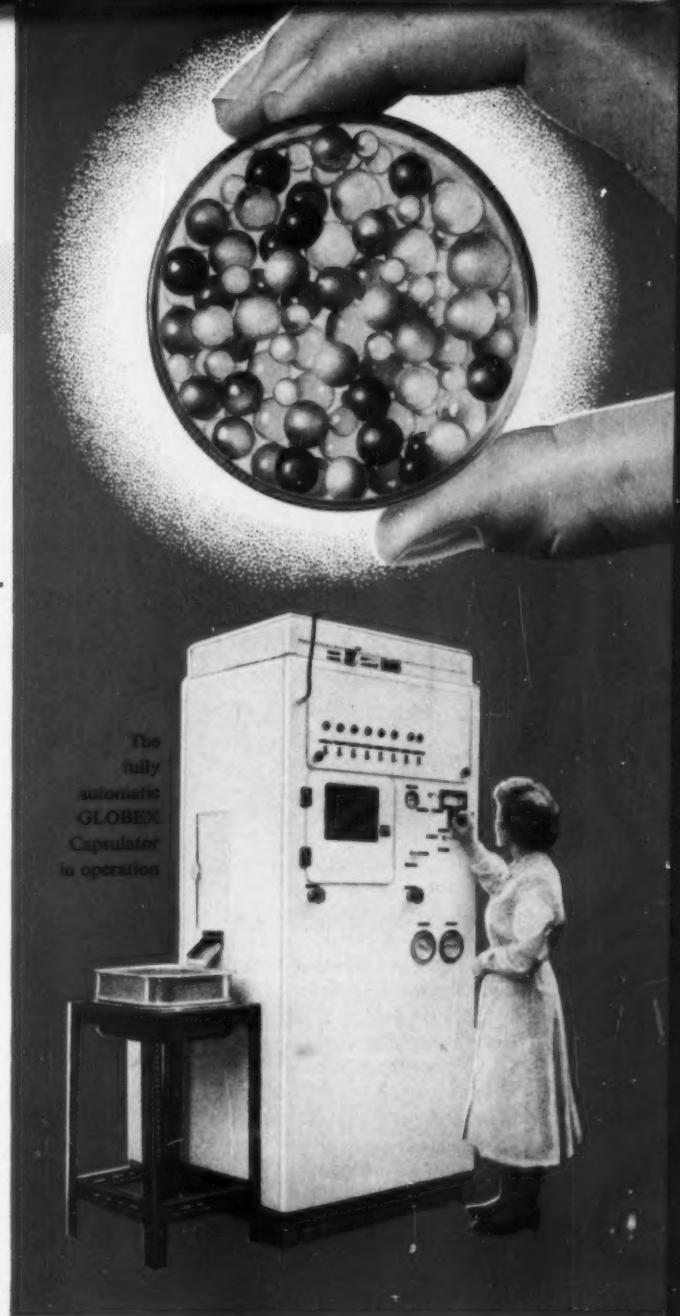
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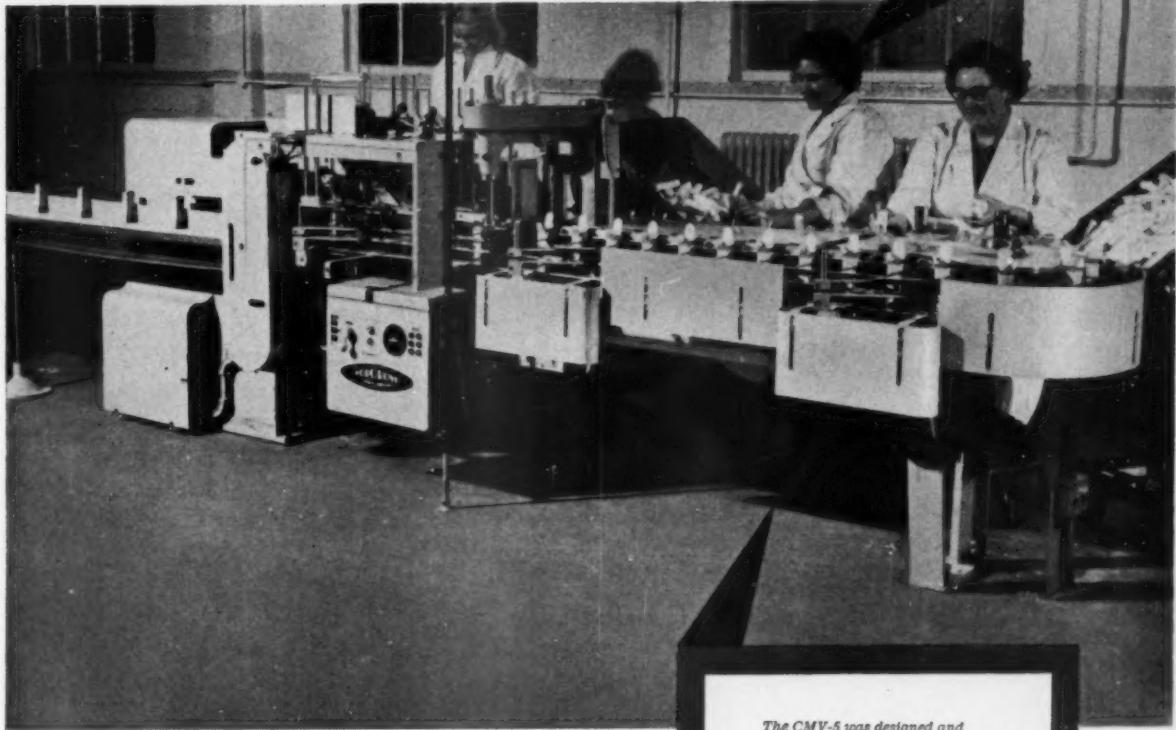
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Barium dihydrogen cyanurate	Hexahydroindane (cis/trans)
Barium hydrogen cyanurate	n-Hexatriacontane
Barium phytate	2-Hexynoic acid
Barium sulphostearate	2-gamma-Hydroxy propyl pyridine
Benzylisothiocyanate	3-gamma-Hydroxy propyl pyridine
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2-Cyclohexane acetic acid	1-Methyl heptylamine-1 (= 2-Octylamine)
4-Cyclohexane butyric acid	2-Methyl hexane
Cyclopentanol-1-carboxylic acid	4-Methyl hexene-1 99%
Cyclohexane-1,4-dione	5-Methyl hexene-1 99%
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Cyclohexyl phenyl ketone	Methyl 2-hydroxycyclohexane carboxylate
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Cyclopentanone cyanohydrin	1-Methyl imidazole
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Embelin (see page 400 of Merck Index 7th)	

# The girls with the CMV smile



These operators at S. Maw, Son and Sons Ltd. of Barnet might well smile—even after a full day's work. For the CMV-5 machine is designed to cut fatigue, to keep them fresh as they load up to 80 surgical dressings a minute into cartons. The CMV-5's secret? *True constant motion.* Because the cartons are transported constantly around the machine, the operators are not disconcerted and fatigued in loading cartons which stop and start, accelerate and decelerate. Even at speeds up to 120 per minute, the movement of inserting the load into the carton is reduced to the minimum. And with both hands free and moving in unison, one operator can load two cartons simultaneously.

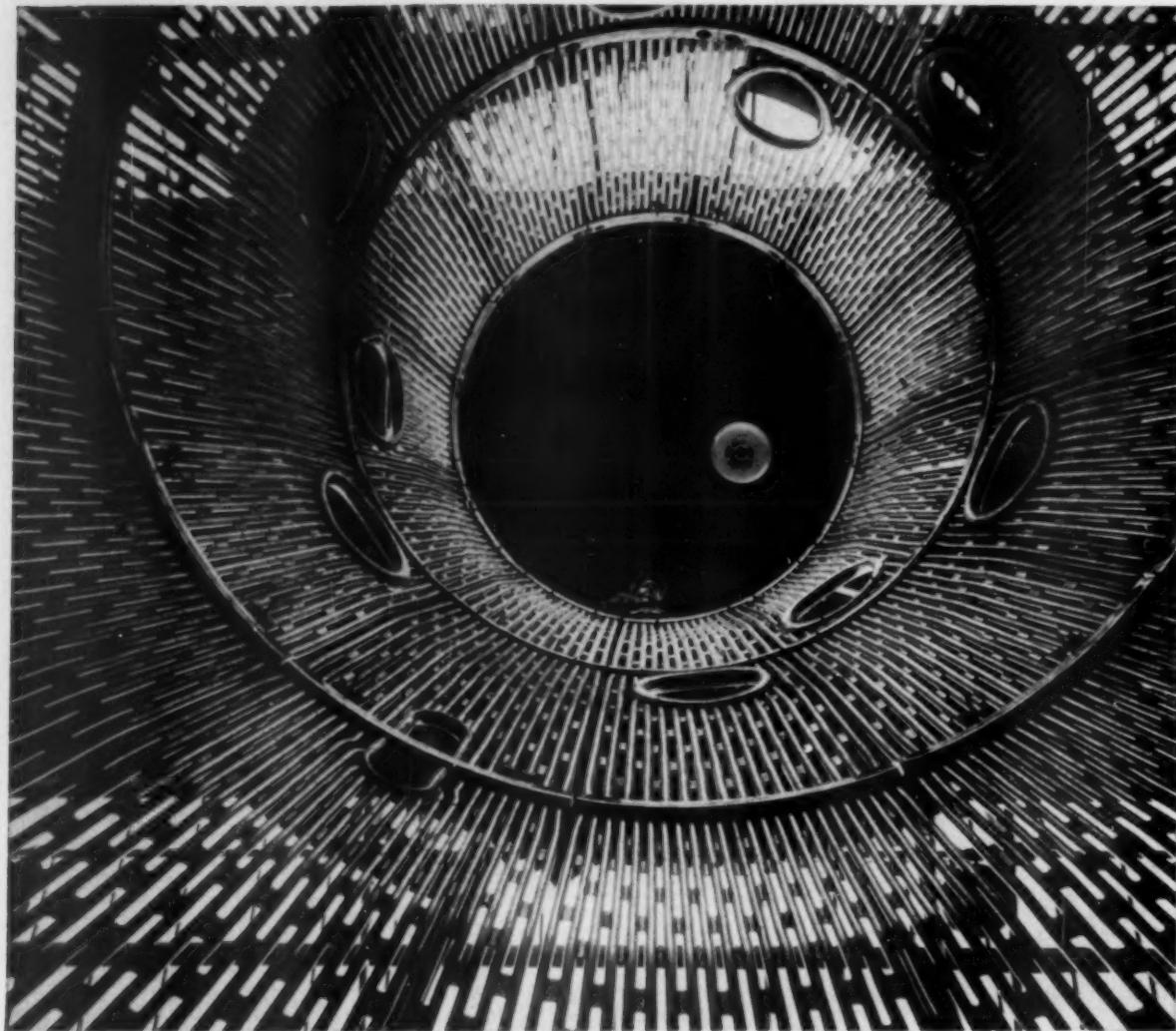
*The CMV-5 was designed and proved by Jones of Cincinnati, is now built in England by Forgrove of Leeds. It automatically forms pre-glued cartons and closes the bottoms and tops. The unit illustrated is part of a packaging line that includes a Forgrove BW-6 machine which overwraps sets of twelve cartons in cellulose film.*

For further details please write to:—

**THE FORGROVE MACHINERY CO. LTD.**

Dewsbury Road, Leeds 11

*A member of the Baker Perkins Group*



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The work was supplied under contract to Whessoe Ltd., of Darlington acting on behalf of the Ministry of Works.

Final erection at site was by Whessoe Ltd. who were jointly responsible with the Ministry of Works for its design.

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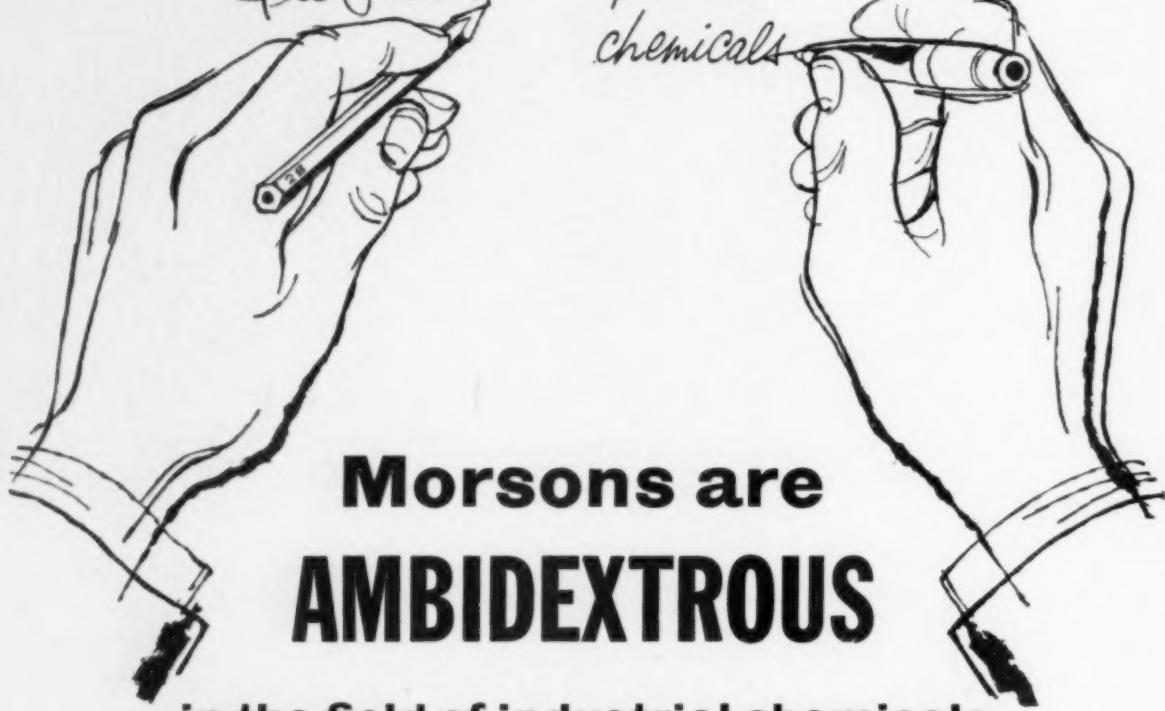
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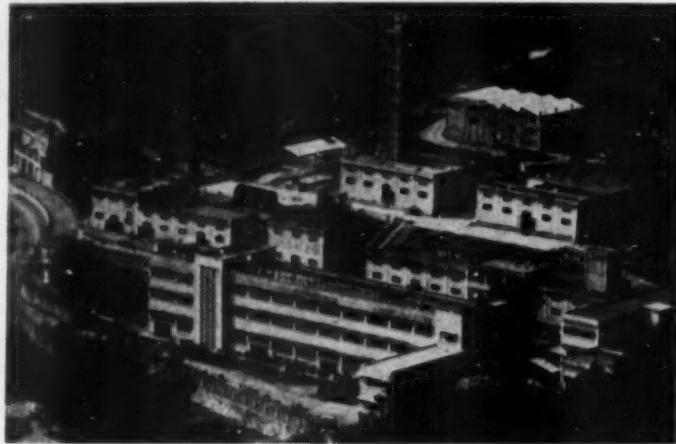
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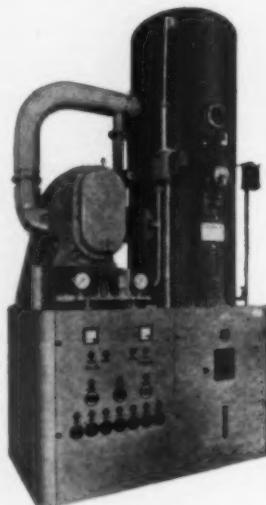


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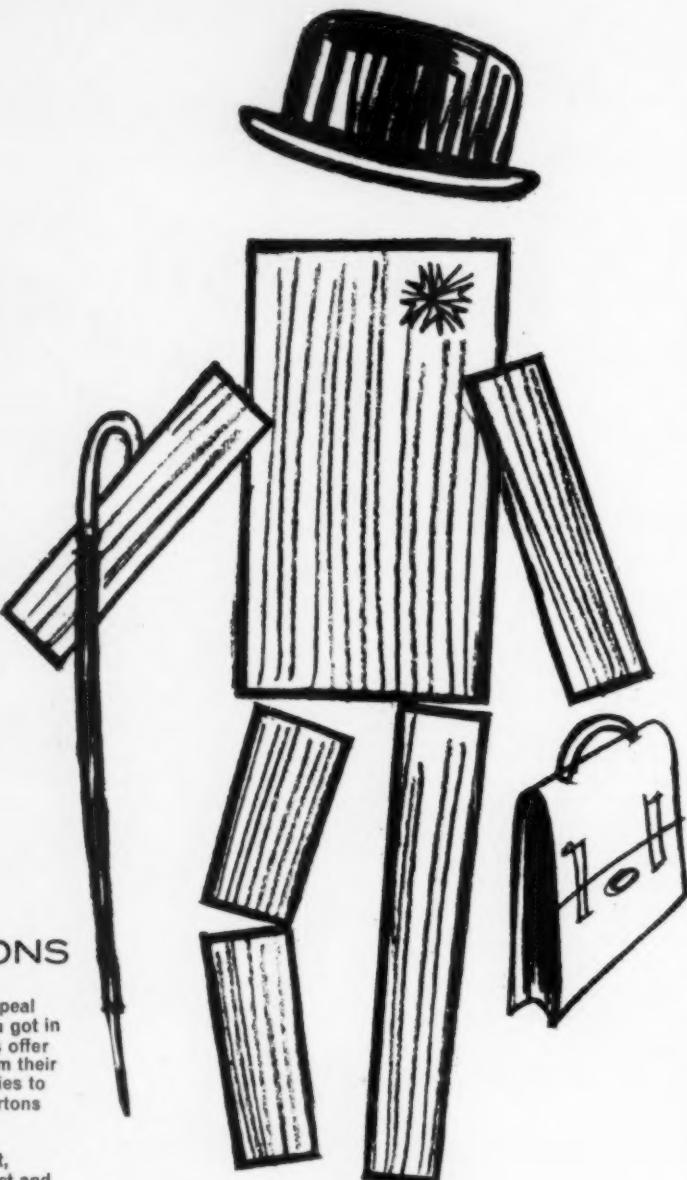
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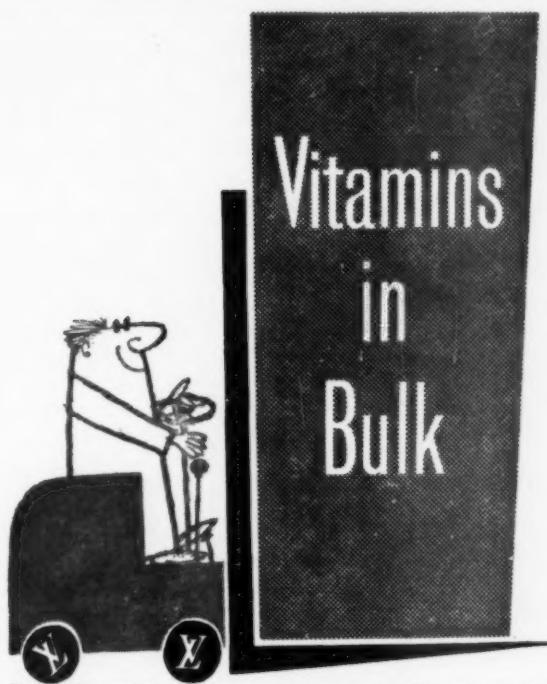


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# Manufacturing Chemist

Editor: W. G. Norris

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NOVEMBER, 1961

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### Pirate imports threaten drug industry

THE THREAT by the Ministry of Health to obtain certain drugs from foreign sources has now become fact by the Government's recent action in which contracts have been placed with four British companies for drugs which will come from manufacturers in Denmark and Italy (see our news pages). It will be recalled that the Health Ministry announced in May their intention of invoking Section 46 of the Patents Act, 1949, in obtaining for the hospital services supplies of certain widely-used drugs—commencing with the tetracyclines, chloramphenicol and the chlorothiazides. Section 46 enables the Government to use patented goods "for the services of the Crown."

It is apparent that the decision was reached with only one idea in mind—to reduce the cost of the N.H.S. bill—regardless of the resulting damage to the pharmaceutical research and exports of this country. It is true that the patentees will be entitled to royalties on these "unlicensed" imported drugs, but these payments will be fixed by the Ministry and not by the patentee. In these circumstances it is unlikely that the payments will bear any relation in amount to the costs of the extensive research from which no saleable products emerge. It is superfluous for these columns to state again the hazards of drug research and the vast cost involved in testing hundreds of compounds before one successful drug is developed. Last year, research expenditure by the U.K. drug industry was £74m. compared with £64m. in 1959 and £3m. in 1954. The Government's action will certainly provide no encouragement for firms to maintain, let alone increase, research expenditure if hospital contracts for their most successful drug discoveries are to be awarded to unlicensed competitors.

Although it is evident that the Health Minister's action will lead to economies in the N.H.S., the loss of patent protection will far offset this action in its effect upon our export trade in drugs; the use of Section 46 of the Patents Act may encourage similar action in other countries.

The treatment of the pharmaceutical industry contrasts sharply with the treatment accorded to another essential British industry—agriculture—supported by subsidies of approximately £260m. per year. If it is considered worth subsidising agriculture by £260m. because, on balance, the country gets value for money, is it not worth paying the drug industry justly for its services rather than importing from pirates to save a few pounds?

What is so amazing is that the Ministry should have taken this step without prior negotiation with an industry which has demonstrated its readiness to determine reasonable prices by its participation

with the Health Departments in a Voluntary Price Regulation Scheme for drugs supplied in the pharmaceutical services.

### Tropical challenge

FACTS about tropical diseases periodically published by the World Health Organisation sharply challenge the skills and resources of the drug industry. While in Western countries infectious diseases have been brought under control, in the rest of the world humanity suffers from parasites, bacteria and other pathogens that cause fearful and disfiguring maladies.

Filariasis is an example. This is a parasitic infection transmitted by mosquitoes which, in its final stages, results in elephantiasis that fantastically distorts the human body. The best drug so far—and it is by no means the complete answer—is diethylcarbamazine. In some circumstances it can obliterate the larva of the parasite from the victim's blood, but unfortunately it does not always kill the female worm, so that in a few months another generation of larva appears if treatment is not renewed.

Other drugs act on the parent worm but not on the progeny. The lack of the perfect drug has led to trials of various treatment schedules. The most promising and most favoured is that of a Franco-American team in Tahiti which seems to show that diethylcarbamazine given in monthly doses, along with mosquito control, is the most rapid and practical way of dealing with and eventually eradicating filariasis.

The W.H.O. has set up an expert committee on filariasis and recently it had its first meeting in Geneva. It reviewed the experience of various field workers and discussed not only drugs but insecticides too. New chemicals are needed to control the mosquito vector (*Culex fatigans*) because it quickly develops resistance to DDT.

No fewer than 200 million people living in the tropics suffer from filariasis. The British drug industry, which has done so much for tropical medicine, has a part to play in defeating this scourge.

### Better safe than sorry

THE methods used by drug companies to persuade doctors to undertake clinical trials of new drugs are severely criticised by an anonymous American doctor in the *Lancet*. He concedes that most new drug developments have stemmed from industry in the past 20 years, but warns his colleagues that any reputation for impartiality or humanitarianism that a drug house acquires is only an incidental by-product of its very clear and natural aim to make profits and sell wares. This, he says, should be firmly



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remembered by any doctor who feels flattered at being asked to take part in a clinical trial of a new substance.

He also warns that the quality of the information given about a new drug is likely to be distinctly variable. In particular toxicity data may be skimped. "There has been a tendency of late for drug houses of all sizes and reputations to become somewhat careless with these toxicity tests, and examples are known where the onus of sub-acute and chronic toxicity has been put in human testing, where it certainly does not belong. The reason for this let-up in safety precautions is partly the flood of new synthetic chemicals . . . which have some activity in the pharmacological laboratory; but it is also due to the willingness of many clinicians . . . to try first and be sorry afterwards. . . During the past five years there have been several examples of premature, faulty, injurious, and fatal drug trials."

The anonymous doctor follows up this serious accusation with criticism of the influence on published clinical results that drug companies seek to exercise by offering, for instance, to "work over" the clinician's statistics or even to write the paper for him. "Even the free supply of drugs for non-paying patients is used by industry as a not so subtle weapon to obtain manuscripts before publication. In a recent case, continuation of drugs for patients was made dependent upon an author's passing across a manuscript (not yet accepted by a journal) to a pharmaceutical company."

How widespread these practices may be in the United States and elsewhere it is impossible to judge, because the author deliberately generalises. But it is not inconceivable that desperate competition among drug companies does generate abuses. At the same time, this competitiveness has produced, and continues to produce, almost all worthwhile medical drugs. Doctors themselves can most effectively stop malpractices by using their professional judgment and knowledge. But the pharmaceutical industry, and not just the American, must recognise that its promotional methods are causing disquiet.

### Bacterial extraction of metals

An unusual example of biochemical engineering is the use of bacteria to facilitate the extraction of minerals from their ores. The National Chemical Laboratory at Teddington found that bacteria influenced the rate of leaching of uranium from columns packed with uranium ore and pyrites. Only 2% uranium was extracted from a sterilised ore-pyrite mixture after 10 weeks' watering, whereas uranium extraction from an unsterilised control column after a similar time was 35%. The influence of oxidising bacteria on leaching rates is further shown by the fact that at 45° to 50°C. there was a sharp decrease in leaching rate and lowering the temperature to 35°C. markedly increased leaching rate. This was due to the activity of the particular oxidising bacteria, *Ferrobacillus ferro-oxidans* and

*Thiobacillus thio-oxidans*, which are inhibited above 40°C.

Similar work has also been reported by the Kennecott Copper Corp. in U.S. Patent 2,829,964. In their process the oxidising activity of bacteria was harnessed to recover copper from mine waste dumps. The naturally occurring species *Thiobacillus ferro-oxidans* was specially bred to withstand 17,000 p.p.m. zinc and 12,000 p.p.m. copper as well as smaller quantities of other metallic substances. In a leach solution containing a low proportion of copper and a high proportion of iron these bacteria oxidise ferrous iron to ferric, which in turn oxidises the cuprous to the cupric state and builds up a concentration of this copper in the leach solution, from which it can be readily recovered. The bacteria are autotrophic and require oxygen and carbon dioxide for growth but no organic materials. They exist in and are tolerant to sulphuric acid. This is a remarkable application of bacteriology to chemical engineering.

### Still corrosion

SEVERE corrosion in distillation equipment can be caused by substances present in only trace quantities. At a corrosion symposium at the University of New South Wales, W. F. Boyling gave the following example. A mixture of acetic acid and ethyl acetate saturated in water was passed into the column, the ethyl acetate-water coming off the top and the acetic acid being taken off from the bottom. A by-product stream containing ethyl acetate, acetic acid, traces of ethyl formate, formic acid and other organic materials was available from another part of the site and was added to the ethyl acetate circuit. It was noticed that each time the column was shut down for cleaning a deep blue-coloured liquid was drained from the reboiler. Inspection of the lower section of the column showed that some bubble caps had been dissolved whilst others were badly corroded.

The main sources of corrosion were thus attributed to traces of formic acid and the problem was solved by replacing the mild-steel column by 18/8/3 molybdenum steel.

This corrosion case history reminds us that the next Corrosion and Metal Finishing Exhibition will be held a year from now—November 27-30 at Olympia, London. This biennial exhibition is sponsored by our associated journal *Corrosion Technology*. From them we learn that already 75% more space has been booked for the next Exhibition than was occupied at last year's. When the remaining bookings are confirmed, the 1962 Exhibition will be twice as big as 1960's, which itself was twice as big as the previous one.

Because of this remarkable rate of growth the Exhibition Organisers have taken the whole of the National Hall at Olympia, an area of 93,000 sq. ft. Lectures and specialist film shows, popular features of the Exhibition, will once again add to the interest and information of the thousands of visitors who come regularly to this well-established display of

anti-corrosion products and services. Manufacturing chemists bothered by corrosion—and who are not?—will find a visit to Olympia instructive and profitable. As soon as next year's diary is available, mark in the dates—November 27-30, Corrosion and Metal Finishing Exhibition, Olympia.

### Drugs versus cancer

ONE of the obstacles to international co-operation in cancer chemotherapy is that pharmacological methods are different in almost every country. This makes it very difficult to compare results and decide which drug is best for different forms of cancer. Hundreds of drugs for the treatment of cancer have been developed in the last 20 years—from nitrogen mustards to periwinkle extracts—so uniformity of pharmacological methods is vital to avoid the present confusion.

This is one of the reasons why the World Health Organisation has set up an expert committee on the chemotherapy of cancer. Their job is to promote co-operation between cancer workers all over the world and to help develop a cancer research programme for the W.H.O. It is certainly necessary to continue to develop new anti-cancer drugs, but equally it is necessary to test existing preparations more thoroughly. That is why uniformity of test methods is so necessary.

W.H.O. is collecting cancer statistics from all parts of the world. In the U.K., for instance, one person in 70 over the age of 45 suffers from cancer. Twenty per cent of all deaths in the U.K. are caused by cancer. Against these depressing figures is the estimate that 28% of all localised forms of the disease can be mitigated or cured either by drugs or drugs plus surgery and radiotherapy.

As to prevention, it is now known that there is a connection between the use of tobacco, and in particular cigarettes, and the marked increase in cancer of the lung among heavy smokers. Cancer may be caused by many industrial products: in the chemical industry these are in particular aniline dyes, which give rise to cancer of the bladder; in metal industries there are cooling mixtures of mineral oils with a carcinogenic effect; and in mining ores containing radioactive substances. Almost everywhere in Europe cancer prevention began with a campaign against these harmful occupational factors and is being continued by the adoption of measures for the prevention of air pollution or by the prohibition of the use of dangerous colouring matter in foodstuffs and in pharmaceutical products or cosmetics such as lipstick.

### Free samples for sale

PHARMACEUTICAL manufacturing and distribution in South Africa seems to be a peculiarly controversial business. Our local correspondent frequently sends reports of squabbles between the various branches of the industry. The latest controversy concerns

doctors. Retail pharmacists complain that their business is suffering because doctors are selling free samples of medicines to their patients. Apparently great quantities of free samples are sent out by members of the Ethical Drug Association. If pharmacists sell their free samples it is regarded as a "normal little bonus." Indeed sometimes the free samples conveniently round out stocks which have to be large to accommodate the vast variety of products on the market. But for doctors to sell their free samples is considered terribly unethical.

It seems a ridiculous situation when so many free samples are distributed that any sort of trade in their selling can be built up. Whether the salesman is a pharmacist or a doctor the sale of free samples is unethical.

### Unsolved problems in pharmaceutics

RESEARCH in pharmacy, as in other fields, has often been done by investigators working under no other pressure than that of an inner compulsion. Much has been achieved by that method, but perhaps more might have been achieved if such research had been correlated and co-ordinated with that of other workers. It is with such a correlation in view that the Department of Pharmaceutical Sciences of the Pharmaceutical Society, under the direction of Dr. Capper, have appointed Science Committees (1) to discover what pharmaceutical research is being done, (2) to collect information on problems requiring investigation, and (3) to find investigators willing to do research work on such problems.

Any research work undertaken in this way would be under the direction of a member of a Science Committee, who would see that the experimental work was properly planned, initiated and effectively pursued.

The scheme has much to recommend it, and it will tend to focus attention on problems of importance, avoid duplication of effort, and stimulate the interest of many who might not be prepared to undertake any research work without some guidance and support.

A list of research projects now being carried out in the schools of pharmacy has been drawn up and broadly classified under the headings of pharmaceutics, pharmacognosy, pharmaceutical chemistry, analysis and pharmacology. Within these classifications there is a great diversity of research products. In pharmaceutics, a considerable amount of work is being done on the physical properties of powders, factors affecting the compression and disintegration of tablets, and a wide range of subjects concerning bacteria and antiseptics. Pharmacognosy is naturally less extensive, but even here the list of research products is impressive. Pharmaceutical chemistry and pharmacology have the greatest scope, but the analytical projects are relatively few.

Some of the problems are particularly suitable for investigation in the schools of pharmacy, whilst

others may appeal to hospital pharmacists. Some workers may prefer to undertake work suggested by the Committee, and the pharmaceutical industry can also play a considerable part in this research programme. Difficulties such as the sharing of patent rights could arise if different organisations had a hand in developing an invention. The committee is aware of this, and preliminary discussions on this point have already taken place.

The Department of Pharmaceutical Sciences is to be congratulated on its enterprise in making this initial attempt to canalise and stimulate co-ordinated research, and such publicity will not only arouse considerable interest, but may bring to official notice a number of problems and ideas worthy of vigorous investigation.

### Iodine makes better lamps

AS POINTED out in an article on another page, the chemical industry has special lighting needs, not the least of which are explosion and flame-proof light fittings. The skill of the lighting engineer can do much to improve the efficiency and comfort of work in chemical factories and laboratories. In return, chemistry does a great deal to improve the efficiency of electric lamps. The development of phosphors is an obvious example of how chemistry helps the lamp engineer. Now that familiar halogen, iodine, seems to be making possible a remarkable breakthrough in lamp technology. We are promised small lamps of wattages equal to those four times as big and of quite exceptional life.

The efficiency of the incandescent lamp increases with operating temperatures, but the hotter a lamp runs the quicker the tungsten filament evaporates. This evaporation, which shortens the life of a lamp, can now be retarded by including within the lamp a trace of iodine. At moderate temperatures the iodine combines with the tungsten vapour to form tungsten iodide. This, in turn, decomposes to tungsten and iodine when it reaches the hotter zone of the filament. The tungsten redeposits on the filament and the iodine is liberated to combine once again with evaporated tungsten. By capturing the evaporated tungsten before it reaches the wall of the lamp, iodine retards the blackening of the lamp. And the useful reaction between tungsten vapour and iodine retards the wasting away of the filament and prolongs the life of the lamp. British lamp manufacturers are hard at work perfecting iodine lamps and during the next year or two they hope to market them.

Meanwhile, in the United States, tantalum carbide is being tested as a replacement for tungsten for filaments of high power lamps. Tantalum carbide filaments are fragile and unstable at high temperatures in conventional nitrogen-argon gas fillings of incandescent lamps. But they perform satisfactorily in a mixed gas of hydrogen, hydrocarbons and halogen acids. Experimental tantalum

lamps have burned for 15 hr. compared to the average 10 hr. life of comparable tungsten lamps, and give 25% more brilliance. This performance makes them promising for projector lamps and also for car headlights and stadium floodlighting.

### Purgatives and privateers

MODERN historians make history more interesting than ever by writing about everyday social and economic affairs. George B. Griffenhagen, formerly curator of medical sciences of the U.S. National Museum, has recorded some fascinating facts about the organisation of medical supplies during the American Revolution. In doing so he throws light upon the origins of the American drug industry.

From the beginning the revolutionaries were short of medical supplies and had little or no domestic industry to help them. Britain was almost the only source and, of course, supplies were cut off when the war began in 1776. To develop trade with other countries was little to the taste of the impatient colonists. They wanted supplies quickly and their privateers seized cargoes from British ships *en route* to New York. Contemporary inventories list considerable numbers of drugs of which about a dozen were desperately scarce. One of the most important scarce drugs was Peruvian bark, the same cinchona from which quinine was later discovered. Tons of bark were used during the Revolution and the price increased more than fourfold between June 1776 and September 1777.

Apparently the diet of the revolutionaries left much to be desired, because there was a terrific demand for cathartics and purgatives. Jalap, ipecac and rhubarb were the galenical favourites, while Epsom and Glauber salts were the chemical choices. Tartar emetic was used for vomiting and cantharides for blistering plasters. Opium was the favourite narcotic, while gum camphor and mercury were used for a variety of purposes.

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An injection of 350 pints would naturally be something of a shock to any patient.



Left: *Erythroxylon coca*, the leaves of which yield cocaine. Centre: *Papaver somniferum*, the opium poppy. Right: *Trichodesma zeylanicum*, a Tanganyikan weed which is the richest source of the alkaloid supinine. It can cause liver damage to grazing sheep.

## New Interest in Medicinal Plants

By Ann Watts,\* B.Sc.

*Interest in plants as sources of drugs has been strongly revived in recent years with the development of reserpine and diosgenin. In Britain the Tropical Products Institute is devoting considerable resources to the examination of plants for pharmacologically active constituents. Here is an outline of their work.*

THE USE of plants and plant extracts in the treatment of disease has been practised since the earliest days of man, and there now exists a vast store of information on the subject, ranging from the ancient Chinese and Indian pharmacopœias to reports of remedies used by witch doctors and medicine men. The names of a number of plant drugs, such as morphine, quinine and cocaine, have become household words, but since their isolation in the nineteenth century research into the production and development of drugs has concentrated on synthesis rather than on testing plants for medicinal activity. As a result, many of the reputed natural drugs have been substantially replaced by synthetic compounds. Over recent years, however, the discovery of new valuable natural drugs and drug precursors such as reserpine and diosgenin has given new stimulus to this field, with the result that the plant kingdom is being carefully

and extensively searched for new medicinal substances. American support for work of this kind has been widely publicised, and the systematic collection and testing of local plants which is being carried out in Australia and South Africa is also well known. It is perhaps less widely appreciated that similar efforts are being made in the United Kingdom. The Tropical Products Institute in London, which has become to a large extent the co-ordinating centre for work of this nature in the United Kingdom, is now engaged in a programme of research on the isolation of physiologically active materials from the plants of tropical areas and maintains close contact with universities and other institutions engaged in similar activities.

### T.P.I. organisation

The primary function of the Tropical Products Institute—a station of the Department of

Scientific and Industrial Research—is to assist the less advanced countries of the tropics and sub-tropics, particularly though not exclusively those of the British Commonwealth, in furthering the development and utilisation of their renewable resources. Its chief concern, therefore, is with materials of plant and animal origin from the tropics and with the industries, local or otherwise, based upon them. Effort is devoted particularly to securing improved processing and extended uses for tropical plant and animal products, including the search for outlets for the waste products of existing industries. The aim of the Institute's work on medicinal plants is to assist development in tropical territories by finding new cash crops which can profitably be cultivated and at the same time to provide new medicinal compounds which can be developed by British industry.

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\* Tropical Products Institute.



Left: One of the laboratories in the new building of the Tropical Products Institute, Grays Inn Road, London; this one is used for research on medicinal plants. Right: Part of the extensive library at the T.P.I.

The Institute has a number of facilities which render it particularly suitable for work of this kind. Its staff of 150 have at their disposal some 20 well-equipped laboratories and a library comprising some 150,000 works on tropical agriculture and tropical plant and animal products, which, with the technical index containing over half a million cards, provide a coverage of this field which is probably unrivalled anywhere in the world. Other facilities include contacts overseas through which plant material is obtained for examination, equipment for carrying out pilot scale extraction of plant material and a pharmacological testing unit financed by the Institute at Birmingham University.

The greater part of the Institute's work arises out of enquiries received from overseas territories, and experts from the Institute make frequent visits overseas to gain first-hand knowledge of local problems in the field of tropical products. Technical aspects of the advisory work are dealt with by specialist sections which cover essential oils, spices, gums and resins; oils, oilseeds, fats and waxes; foods and feedingstuffs; fruits, fruit products, vegetables, edible nuts and flowers; pesticides; drugs; fibres; paper and board-making; hides, skins and tanning materials; power sources (particularly solar energy, but excluding conventional sources of power). Economic problems featuring in enquiries are handled by the Economics and Statistics Section, which also conducts market surveys of selected products and groups of commodities of importance to the tropics. The technical and economics sections work in conjunction to answer enquiries, and carry out laboratory investigations where necessary, on the selection of new

crops, cultivation, processing, preparation and preservation methods, quality control, use of waste products, packing, transport, marketing, etc.

In addition to this advisory work a certain amount of long-term research is carried out in the laboratories of the technical sections. A number of laboratories, however, are devoted almost exclusively to research of a more fundamental nature on tropical products, and it is here that research on the isolation of physiologically active materials from plants of tropical areas is being carried out.

#### Choosing plants for study

The first stage in work of this kind is to select plants for examination, and this alone can prove a major operation. The methods employed for this purpose include literature searches to find plants used locally for medicinal purposes and as poisons, including fish, dart and arrow poisons, and the study of those plant families known to contain many species rich in useful chemical constituents, such as the *Apocynaceae* and *Solanaceae*. Unfortunately the elimination of plants which have already been investigated and the selection of promising plants on which to work is rendered more difficult by the fact that research in this field has been reported in the journals of a wide range of disciplines, including botany, chemistry, medicine, pharmacology, agriculture and anthropology. Moreover many of the books which have been written on the subject of local medicinal plants contain information which has been gathered largely by hearsay and is therefore dubious. The method most widely used by workers in this field, therefore, is to carry out simple spot tests for substances that are likely to be of

interest, such as alkaloids and saponins, on all the plant species which can be collected in any particular area.

The second stage, obtaining the plant for examination, is greatly facilitated by the Institute's service of providing plant material from the tropics for research purposes. This is made possible by the co-operation and invaluable assistance rendered by contacts in overseas territories who go to considerable trouble to collect the plant material required, and by this means the Institute is able to obtain plants from almost any part of the world. Large numbers of plant samples are obtained in this way, and supplied not only to sections within the Institute itself but also to research workers in universities, pharmaceutical firms and research institutions in the United Kingdom and, to a small extent, overseas.

#### Preliminary screening

In the past two years several hundred plants have been subjected to spot tests for alkaloids and saponins at the Institute, and a number of alkaloid-containing plants selected in this way are now being examined further. Aqueous extracts of selected plants are prepared at the Institute and submitted to screening at the pharmacological unit at Birmingham University. The screening, carried out on experimental animals, includes acute toxicity tests and subsequent determination of mode of action, tests on a range of standard organ preparations and other tests where necessary. Further chemical work is largely based on the results of these initial tests, and plants showing promising biological activity are subjected to more detailed study at the Institute, their active principles being isolated and characterised



chemically and biologically. It is intended to make structural studies of any substances isolated which have outstanding value and whose constitution is unknown.

In addition to the routine screening described above, plants are also examined at the Institute as a result of a specific request or because definite indications are received as to their promising nature in this work. The seeds of *Trichodesma zeylanicum*, a weed which occurs in Tanganyika after the harvest, were being considered as a source of oil, and samples were sent to the Institute for examination. About 2% of alkaloids on a dry weight basis were found, the major alkaloid being supinine in quantities showing this plant to be the richest known source of this alkaloid. Supinine is known to cause chronic liver damage leading to death in sheep, so that while the investigation did not lead to the discovery of a valuable new medicinal compound, it did enable the Institute to warn the authorities in Tanganyika of the danger to livestock grazing on this weed.

#### Contract research

Research on medicinal and poisonous plants is also carried out under contract for the Institute by a number of universities and colleges in the United Kingdom and overseas. This includes the investigation of steroid and triterpenoid constituents of East African plants, in the Department of Chemistry, Makerere College, Uganda; the chemical investigation of plants of Hong Kong Island and the New Territories, in the Department of Chemistry, University of Hong Kong; the investigation of *Strychnos toxifera* alkaloids, in the Department of Organic Chemistry, University of Bristol; the investigation of alkaloid constituents of some Colonial and Commonwealth plants, in the Department of Chemistry, Manchester College of Science and Technology; and the study of steroid sapogenins from *Dioscorea* species, in the Department of Pharmacy, Nottingham University.

As with plants examined at the Institute, extracts of plants which are investigated extramurally are also submitted to testing at the pharmacological unit at Birmingham where necessary. This is particularly so with the work of the Natural Products Research Unit in the Department of Chemistry, University College of the West Indies, where



**Meticulous preparation of pyrethrum flowers for examination in the T.P.I. laboratories. The introduction of this profitable crop into Kenya was a direct result of the encouragement given in the late twenties by the Imperial Institute, forerunner of the T.P.I.**

local poisonous and medicinal plants, including the West Indian "Bush Teas," are being investigated with the object of finding new pharmacologically active substances and also establishing the toxicity of certain local plants. Standard extracts of some 100 plants have so far been prepared and submitted to pharmacological testing, and a number of promising plants are now being subjected to more detailed investigation.

Any naturally occurring substances of outstanding medicinal value which come to light as a result of these investigations and are considered to be of commercial interest will, where possible, be patented by the Department of Scientific and Industrial Research. Patent rights will be assigned to the National Research Development Corporation, which will then be responsible for further development and commercial exploitation.

#### Corticosteroid source

In collaboration with pharmaceutical firms in this country the Institute has for some time been investigating the plant genus *Dioscorea* (yams), many non-edible species of which contain diosgenin. Diosgenin is not itself physiologically active, but is the starting material for one of the two commercial processes at present in operation in the United Kingdom for the production of the cortico-steroid group of drugs. It is not yet possible

to synthesise the steroid ring economically, and diosgenin is therefore a very valuable precursor in the preparation of drugs which would otherwise have to be obtained largely from inadequate animal sources. Present supplies of diosgenin in this country are obtained mainly from a few wild plant species in Africa and Central America, and as the demand for diosgenin is likely to increase within the next few years a new and controllable source of the substance is urgently needed.

Numerous *Dioscorea* species from a variety of localities have been examined at the Institute for their diosgenin yield, including a number of species collected in British Honduras by a member of the Institute staff. Analyses indicate that at least one of the latter species holds promise for commercial exploitation, and this yam is now being grown in trial plantations in British Honduras in order to determine whether its large-scale cultivation in this area for corticosteroid production would be a practical proposition. Similar cultivation trials of high yielding *Dioscorea* species are also being carried out in East Africa to assess their suitability for introduction as new cash crops.

#### Pyrethrum

As has already been stated, the principal aim of the Institute's work on medicinal plants is to find new cash crops which can profitably be cultivated by the underdeveloped countries of the tropics. An outstanding example of the effect which the successful introduction of a crop can have on the economy of a territory is provided by pyrethrum, the insecticide with which, for many years, the Institute has been closely concerned. In the late 1920s a Kenya farmer consulted the Imperial Institute, of which the body now known as the Tropical Products Institute was then a part, with regard to high-priced crops that might be suitable for cultivation on his plantation in Kenya. At that time there was a growing demand for pyrethrum, market prices were favourable, and a British source was highly desirable as an alternative to the Japanese industry which then dominated the world's supply of the insecticide. As it seemed probable that certain areas in the Kenya highlands would be suitable for cultivation of the plant, and

(Continued on page 502)

# Small-scale Processing Machinery

Though few pharmaceutical products can be made without mixing there is surprisingly little theoretical basis for the mixing operation. Here Mr. Fowler defines the fundamentals of liquid mixing and describes the four main types of mixing apparatus.\* In further articles he will deal with powder and solid mixers.

## MIXERS

### I. Liquid Mixers

By H. W. Fowler,<sup>†</sup> B.Pharm., F.P.S.

IT IS difficult to find a single pharmaceutical product where mixing is not necessary in some stage of the process. So it may appear surprising that there is little or no theoretical basis to the mixing operation. This arises from the fact that many types of materials having greatly different properties have to be mixed. These materials may range from mobile, readily-miscible liquids to suspensions of solids, which may reach semi-solid consistency, and also to mixtures of powders. Because of this variety of materials no general means of assessing the degree of mixing is possible, the methods which have been proposed being of limited application to certain substances only. As a result of this, mixers have developed empirically for particular purposes and a great number of different types are available commercially, some of which are versatile while others are designed for specific uses.

To make any classification of mixers possible, we must consider what is meant by "mixing" and the influence of the various types of substances to be handled.

#### Definition and objectives of mixing

Mixing may be described as an operation in which two or more ingredients existing in a separate or roughly mixed condition are treated so that each particle of any one ingredient then lies as nearly adjacent as possible to a particle of each of the other ingredients.



Fig. 1. Stirrer with variable transformer control.

This theoretical degree of mixing is rarely possible (the blending of miscible liquids of low viscosity is the only instance), is frequently unnecessary and, in some cases, is undesirable in practice (an illustrative example of the latter is in liquid/liquid extraction, for example in antibiotic manufacture, where a temporary dispersion only is required and a too intimate mixture would give rise to separation problems at later stages).

How nearly the mixing should attempt to approach this theoretical ideal will depend upon the purpose of the product, and the objectives of mixing may be broadly classified as follows:<sup>1</sup>

1. *Simple Physical Mixture*—the production of a blend of two or more miscible fluids or two or more uniformly divided solids. In pharmaceutical practice the degree of mixing required is commonly of a high order, as many such mixtures are dilutions of potent substances and correct dosage must be assured.

2. *Physical Change*—to effect a change which is physical as distinct from chemical, for example the solution of a soluble substance. In such cases a lower efficiency of mixing is often acceptable, as solution would occur by diffusion, without agitation, but mixing accelerates the process.

3. *Dispersion*—the mixing of two immiscible fluids or a solid in a fluid. A special case of the former is the preparation of emulsions, which has been considered already in this series ("Emulsifying Machinery," March 1961). The latter is commonly used in the preparation of suspended mixtures, pastes, etc.

4. *Promotion of Reaction*—mixing will frequently encourage (and at the same time control) a chemical change, so ensuring a uniform product, examples being the manufacture of products involving adjustment to pH or making articles such

\* Seventh in the MANUFACTURING CHEMIST series. 1. Emulsifying Machinery appeared in March, 2. Mills and Sieves in April, 3. Tabletting Machinery in May, 4. Mechanical and Convection Dryers in June, 5. Conduction and Radiation Dryers in July, and 6. Filters in September.

<sup>†</sup> Senior Lecturer in Pharmaceutics, School of Pharmacy, Leicester College of Technology and Commerce.

as Solution of Ammonium Acetate. Danckwerts<sup>2</sup> suggests the division of mixtures into three types, which differ fundamentally in their behaviour:

1. *Positive Mixtures*—for example gases or miscible liquids—are those where irreversible mixing would take place by diffusion, without the expenditure of any work, provided that time is unlimited. Generally such materials do not present any problems in mixing.

2. *Negative Mixtures*—for example suspensions of solids in liquids. Such mixtures require work for their formation and the components will separate unless work is continually expended on them. Generally speaking, such mixtures are more difficult to obtain, so that a higher degree of mixing efficiency is required.

3. *Neutral Mixtures* are static in their behaviour, the components having no tendency to mix spontaneously, nor do they segregate when mixed. Many pharmaceutical products are examples of this class, including mixtures of powders, pastes, suspensions of solids in thixotropic liquids (e.g. Calamine Lotion, B.P.).

It will be apparent that within these main groups variations will occur owing to different physical properties of these materials. Such

factors will include viscosity (and any changes of viscosity during the mixing), specific gravity, the relative gravities of the components, particle size, ease of wetting of solids and surface tension of liquids, while other factors such as the proportions of the components and the required order of mixing will exert an influence.

For the purposes of considering small-scale equipment, mixers will be divided into three main groups:

1. "Liquid Mixers" for positive and negative mixtures, where the liquids involved are simple or "Newtonian."

2. "Powder Mixers" for neutral mixtures, where the components are solid, particulate materials.

3. "Solid Mixers" for dealing with neutral mixtures, where the product is of semi-solid consistency and the liquids are commonly complex or "Non-Newtonian."

Liquid mixers will be considered in this part and powder and solid mixers in subsequent articles.

#### Fundamentals of liquid mixing

All mixing operations have two basic requirements, which may be achieved in various ways:

1. Localised agitation, sufficient to give the required degree of mixing in the immediate neighbourhood of the mixing element.

2. A suitable rate and direction of movement of the whole bulk of the material, so that all will pass through the intense mixing area, to give uniformity of the final product.

In general, flow alone is insufficient to give adequate mixing, as it is possible for streamline flow conditions to prevail and for stratification of liquids or settling of solids to occur. Certain mixers, however, do rely on vigorous movement of the container to produce turbulent flow conditions and so to achieve mixing, but it must be remembered that this method is effective only if shearing forces are not necessary, for example if mixing is to assist dissolution. This is illustrated by the fact that an emulsion can be prepared by shaking in a bottle, but such preparations are usually unstable. To produce a stable product homogenisation is necessary, that is the application of shear forces to the mixture to reduce the globule sizes.

Thus, if versatility is required mixers will need a mixing element, commonly a rotational device, with the object of providing the necessary shear forces for the local mixing,

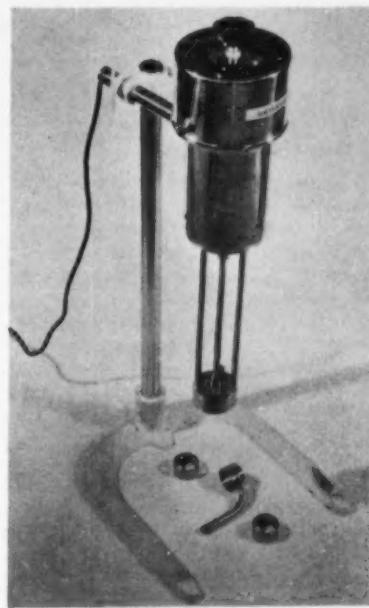


Fig. 3. General purpose laboratory mixer for liquids.

but also capable of acting as an impeller to set up the necessary flow pattern.

Certain general principles of mixer design have been suggested,<sup>3</sup> relating the mixing element speed and size to the apparent viscosity of the liquid.

Firstly, as the apparent viscosity of the materials increases, the optimum speed of rotation of the mixing element decreases:

$$\mu_a \propto \frac{1}{n} \dots \dots \dots (1)$$

where:  $\mu_a$  = apparent viscosity  
 $n$  = speed of rotation of mixing element

Secondly, as the viscosity of the material increases, the ratio of the diameter of the container to the diameter of the mixing element decreases:

$$\frac{1}{\mu_a} \propto \frac{D}{d} \dots \dots \dots (2)$$

where:  $\mu_a$  = apparent viscosity  
 $D$  = diameter of container  
 $d$  = diameter of mixing element

Equation (2) arises from the fact that increasing viscosity denotes increasing resistance to flow. Hence, the mixing element cannot impart the necessary energy to the material to set up a flow pattern reaching to all parts of the container, so that a larger mixing element is used to extend the area of localised mixing. Thus, for liquids of low viscosity, a high speed mixing element with a  $D/d$  ratio of about 20 is suitable.



Fig. 2. Propeller mixer for the range 2-25 gal.

With liquids of higher viscosity, the  $D/d$  ratio is decreased until, in the case of pastes, etc., the mixing blades rotate slowly and scrape the container sides, *i.e.*  $D/d=1$ .

#### The intense mixing zone

In the case of high-speed mixing elements the use of a rotating disc or discs will cause high localised shear forces, but such units are not widely used as the liquid flow caused by the disc is slight. In practice, therefore, a compromise must be made and the element must give rise to shear forces, but also be capable of setting up a flow pattern; marine type propellers or bladed turbine impellers are commonly used.

As an alternative to rotation, a rapid oscillatory movement of the element may be employed and a vibrating perforated metal disc will give rise to the necessary shear forces, while tapering of the perforations will cause liquid flow.

Slower mixing elements usually consist of flat blades, the blade being arranged perpendicularly to the direction of movement. Hence considerable eddy formation will occur and the intense mixing zone is, therefore, to the rear of the blades.<sup>4</sup>

#### The flow pattern

The velocity of the liquid in the container at any point will have three components and the complete flow pattern will depend upon variations in these components in different parts of the container.<sup>5</sup>

The three velocity components are:

1. A radial component, acting in a direction perpendicular to the impeller shaft.
2. A longitudinal component, acting parallel to the impeller shaft.
3. A tangential component, acting in a direction tangentially to a circle of rotation round the impeller shaft.

Since small-scale mixers normally use a vertical shaft, it follows that the longitudinal component will be in the vertical plane and the radial and tangential components in the horizontal plane. A satisfactory flow pattern will depend upon the correct balance of these components.

Excessive radial movement, especially if solids are present, will take the materials to the container wall, whence they fall to the bottom and may rotate as a mass beneath the impeller, so causing segregation instead of mixing.

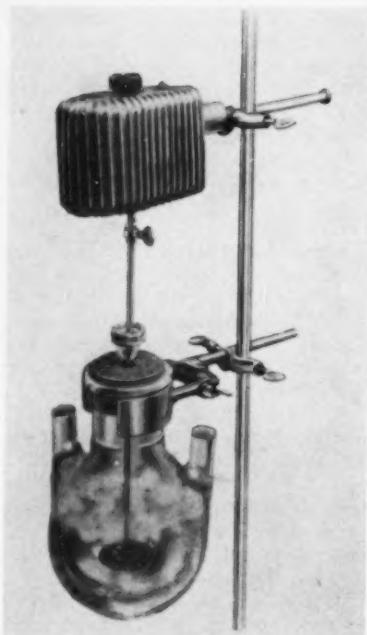


Fig. 4. Mixer driven by vibrator operating on a.c. current to give 6,000 strokes/min.

If the tangential component dominates, a vortex is formed and this may deepen until it reaches the impeller, when considerable aeration occurs.

When the longitudinal component is insufficient, it is possible for liquid and solid, or two liquids of differing specific gravities, to be carried round in streamline conditions, remaining unmixed. This stratification may occur when rotation is rapid and in the presence of vortexing, when there is every appearance of vigorous mixing.

It will be obvious that container shape will have an influence on flow pattern. The most commonly used vessel is cylindrical and central mounting of the impeller gives a symmetrical arrangement which enhances vortexing. This may be prevented by two methods.<sup>6</sup> Firstly, the impeller may be mounted "off-centre" or with the shaft inclined to the vertical. Alternatively, baffles may be introduced, which must not be too wide or dead spots may be formed. Baffles may be vertically on the walls or as a cruciform baffle on the bottom of the vessel. A further possibility is to use a "push-pull" propeller, that is, to have two propellers of opposite pitch on the same shaft, which counteracts the rotational effect and throws upward

and downward currents of liquid together.

The use of containers other than cylindrical will reduce rotational swirling and vortexing, but may give rise to dead spots, for example, in the angles of rectangular vessels.

#### TYPES OF LIQUID MIXERS

Liquid mixers may be divided into four main groups, the first consisting of the shaker type, where the container is agitated, while the remainder employ a mixing element, *viz.*, propeller, turbine or paddles.

Each type has advantages, uses and characteristics, particularly in terms of the viscosity of the material for which the mixer is suitable, propellers, turbines and paddles being suited to increasing viscosities, in that order. For this reason paddles are used most frequently for viscous materials and pastes and will be considered in a later article.

#### Shaker mixers

Shaker mixers are generally applicable to very small-scale working only, the agitation of anything other than a small container presenting handling problems.

Bottles or flasks up to 500 ml. capacity may be agitated in vertically oscillating shakers, giving a movement comparable with hand shaking. Larger containers, for example Winchester quart bottles, may be shaken in a horizontal oscillating shaker.

#### Propeller mixers

Propeller (or helical impeller) mixers are probably the most widely used of small-scale mixers, but are frequently not employed to their maximum efficiency.

The propeller may be small in relation to the container (a propeller/container ratio of 20 being satisfactory) and operates at high speeds, up to 7-8,000 r.p.m. The propeller accentuates the longitudinal movement of the liquid and is therefore most suitable for liquids where the energy imparted by the propeller to the fluid is sufficient to set up a satisfactory flow pattern. The propeller is not normally effective with liquids of viscosity greater than about 5,000 centipoises, which is somewhat greater than the viscosity of glycerin or castor oil.

Propellers used on bench scale equipment may be fully shaped, as in marine propellers, or may be more simply made by twisting

blades in a disc of sheet metal. In general, the latter will give rise to higher shear forces, but will have a variable efficiency of directional movement of the liquid.

In use, it is important that—

1. The propeller should be deep in the liquid. If near the surface, vortexing is more likely to occur and the flow pattern may leave dead spots at the bottom. Peck<sup>3</sup> recommends that the propeller should be not closer than one propeller diameter from the bottom and should be covered by a liquid depth equal to twice the propeller diameter at low speeds and four times the diameter at high speeds.

2. The propeller should be off-set or mounted at an angle, in order to reduce vortexing and aeration. Alternatively, a vertical baffle may be used and, on the bench scale, may be improvised from a spatula held in a clamp stand.

It must be emphasised that rapid rotation with swirling, vortexing and aeration should not be allowed to take place—such conditions appear to be turbulent, but this is not necessarily the case.

The propeller will perform most mixing duties when used correctly, but the longitudinal movement imparted by a propeller makes it the best unit to use when strong vertical currents are required, as in the suspension of solids in a liquid. It is not ideal when considerable shear is needed, as in emulsification.

#### Turbine mixers

The turbine mixer has an impeller with a number of short vertical blades, which may be straight or curved. The turbine impeller is usually rotated at a somewhat lower speed than the propeller and the impeller/container ratio is lower, the desirable value depending upon the viscosity of the fluid (see equation (2)).

The blades may have a pitch, giving some axial flow, but most turbine impellers use flat blades. In such cases there is very little axial or tangential flow, the liquid being moved rapidly in a radial direction. Turbine type impellers give rise to greater shear than propellers and this can be increased further by fitting a diffuser ring. This is a stationary perforated or slotted ring, which surrounds the impeller, so that the discharged liquid must pass through the apertures. The diffuser reduces rotational swirling and vortexing, but

is most useful in increasing the shear forces.

Turbine mixers are satisfactory with mobile liquids, but can deal with more viscous liquids than the propeller mixer, having a range up to 100,000 centipoises—approximately the consistency of molasses.

The absence of marked vertical flow means that the standard turbine mixer is less suitable than the propeller for suspending heavy solids, although special heads may be fitted to commercial models. The higher shear forces and the greater viscosity range give it a special application in the mixing of liquids which may stratify with a propeller and, particularly, the preparation of emulsions of immiscible liquids.

#### Vibratory mixers

As an alternative to rotation the impeller may be vibrated at a high frequency, for example by means of alternating current, so giving 6,000 strokes per minute on the usual mains frequency. The impeller may take various forms but is commonly a perforated disc, with the holes tapered so that axial flow occurs. This flow, together with the shear arising from the vibration, results in efficient mixing. Such mixers do not rotate and vortexing is not a problem; the absence of rotary movement also means that the shaft can enter a closed container without the need for a special gland, a simple membrane of inert material being sufficient. The method is therefore suitable for sterile conditions.

#### COMMERCIAL MIXERS

The following pieces of apparatus are available commercially and illustrate the various classes referred to above.

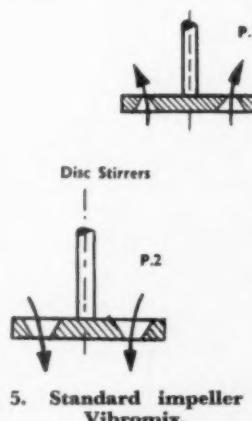


Fig. 5. Standard impeller for Vibromix.

#### Oscillating shaker

The Griffin and George silent shaking machine has a cradle which will accommodate two Winchester quart bottles, held in a horizontal position. Adjustable supports enable smaller bottles or containers to be shaken.

The frequency of the oscillation is 275-280 strokes per min., but the amplitude is variable and may be set at  $\frac{1}{2}$ , 1 or  $1\frac{1}{2}$  in. Special bearings avoid bearing play and rattle and the design is such that rapid acceleration is obtained on each stroke. Long, slow strokes will cause only gentle "slopping" of the contents, with little mixing, but short, rapid strokes give vigorous agitation and greater mixing efficiency.

#### Flask shaker

The Griffin flask shaker will accommodate four flasks or bottles of 500 ml. capacity, each half full of liquid. Shaking is normally in a vertical plane, but the side arms may be rotated to alter the angle of shaking. A potentiometer enables the frequency to be varied continuously from zero to 500 oscillations per min., giving agitation comparable with vigorous hand shaking.

Modified side arms may be fitted, increasing the capacity to eight flasks. It is important to remember that the load must be balanced, which may be a disadvantage if the shaker is required for varied dispensary work.

#### Bench-scale stirrer

Laboratory type stirrers have been described in this series already ("Emulsifying Machinery," March 1961), with the Mitchell stirrer quoted as an example. A great many units are made over a considerable price range and are available from every laboratory equipment supplier. Almost all have speed control, but the majority use a variable resistance, which brings the disadvantage of loss of torque at low speeds.

The Anderman stirrer (Fig. 1) overcomes this difficulty by the use of a variable transformer control for the  $\frac{1}{60}$  h.p. motor, with the voltage to the armature of the motor being controlled by means of an autotransformer with multiple tappings, while the field windings are supplied with full mains voltage. This arrangement gives high torque at low speeds, which is a great advantage when a variety of materials, needing different con-

ditions, have to be handled. Furthermore, autotransformer control gives constant speed at any setting, whereas the speed alters with resistance controlled motors as the resistance heats up; this is a useful point when uniform conditions are required for a number of batches, as in development work. The unit is also suitable for prolonged use as, unlike the resistance control, the transformer does not heat up or burn out.

It will be seen from Fig. 1 that the autotransformer has two controls, the first graduated between 0 and 100 and the second between 0 and 10, each with 10 positions. Thus, there are 110 possible settings between zero and maximum speed.

The illustration also shows the reduction gear which may be fitted, giving a speed reduction of 11 : 1, so that the apparatus may be operated at any one of 220 speeds, between 50 and 7,000 r.p.m. The shaft is double ended, enabling the unit to be used for driving other apparatus.

Stirrers of  $\frac{1}{2}$  in. shaft diameter are fitted into a chuck and various shaft lengths and agitator diameters are available (in glass and stainless steel) as well as a collapsible unit for use in flasks or bottles.

The apparatus is well made but of low cost, the total price for the motor, controller, reduction gear and chuck being less than £15, with agitators extra according to requirements.

#### Mobile mixer

The term "small-scale" frequently involves quantities larger than can be handled on the bench, and the propeller mixer made by Chemical Equipment Engineering Ltd. is an example of the type of plant suitable for working in the range 2-25 gal., or even larger quantities, depending upon the materials. The model illustrated in Fig. 2 has a  $\frac{1}{4}$  h.p. motor, operating at 1,440 r.p.m. The propeller and shaft, of stainless steel, are attached by a bayonet fitting allowing easy removal and cleaning. Other variants of power, speed and materials of construction may be obtained if required.

The mixer is fully mobile, moving on ball-bearing castors, with adjustable feet which screw down when the mixer is in position to ensure steady operation. Vertical adjustment may be effected very simply over a range of 2 ft., as the motor

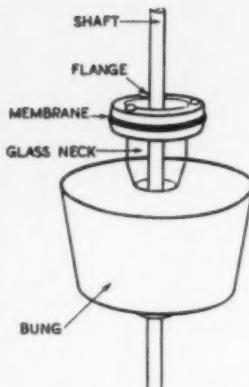


Fig. 6. Membrane sealing unit for Vibromix.

is accurately balanced by a counter-weight within the tubular stand, a locking device preventing movement when in operation.

No provision is made for altering the angle at which the mixer may be operated, the motor being mounted permanently with the shaft inclined at an angle of  $10^\circ$  to the vertical, but this is a satisfactory angle in most cases. The tubular stand has a key which prevents rotation of the mixer on its vertical support, but the propeller position in the container may be altered by moving the entire mixer relative to the vessel.

#### Silverson mixer

A commercial example of the turbine mixer is the Silverson mixer, the laboratory model of which is illustrated in Fig. 3, from which it may be seen that the impeller, which has four radial blades, may be surrounded by a diffuser, that is, a suitable head or mesh according to the materials to be mixed. This gives considerable versatility, enabling high shear forces to be obtained when necessary (e.g. for homogenisation), or by the use of the disintegrating head to effect dispersions of materials such as gums, or by fitting axial flow heads or pump heads where the emphasis is to be placed on flow (e.g. to maintain solids in suspension).

The Silverson Mixer is probably the most useful general-purpose mixer for liquid media, having many applications with a wide range of materials.

#### Vibrating mixer

The Vibromix (Fig. 4) is driven

by a vibrator operating on alternating current, so giving 6,000 strokes per min. on the usual 50 cycle supply. The length of stroke is short, having a maximum of about  $\frac{1}{6}$  in., but the amplitude may be regulated continuously down to zero. The vibratory unit is completely enclosed and so is dust, liquid and vapour proof, and, as no rotation occurs, bearings and glands are unnecessary. A wide variety of impellers is available to give rotational movement, pumping, circulation, aeration, etc. The standard impeller consists of a perforated disc, with the holes tapered as shown in the sectional diagram (Fig. 5). The vibratory movement produces shear forces and the taper of the perforation causes flow, which may be upwards or downwards, according to the direction of the taper. Discs of various sizes and with different diameters and numbers of holes are available in Pyrex glass or stainless steel.

If the Vibromix is used in connection with a membrane sealing unit (see Fig. 6), the mixer may be used in a container which is completely closed, e.g. under sterile conditions. Membranes are of Neoprene synthetic rubber normally, but may be of other materials, such as P.T.F.E., for special circumstances.

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**Fire protection in industry.** In order to help managements at all levels check their fire protection measures, the Fire Protection Association has published a "Check List for Fire Safety in Industry," containing about 40 questions on the fire safety of their premises. The leaflet includes questions on fire precautions relating to machinery, heating and lighting equipment, flammable liquids and smoking. There are also sections which emphasise the importance of cleanliness and tidiness, the proper storage of goods and recommend measures to restrict damage in case of fire.

# Cosmetic and Perfumery

## RAW MATERIALS REVIEW

**V. Vasic, C.H.E.**, makes an assessment of new and improved raw materials for cosmetics, perfumery and toilet preparations. His last review appeared just over two years ago (October 1959) and since then most suppliers have developed new materials. Among the products reviewed are detergents and surface active agents, lanolins, fatty acid derivatives, gland esters, powders, deodorants, silicones, floral perfumes, synthetics, musk and sandalwood substitutes.

### COSMETIC MATERIALS

#### Detergents and surface active agents

A new series of detergents—*Texapons*—have been developed (Dehydag). *Texapon MG 1214* is magnesium salt of a lauryl-myristyl alcohol sulphate. *Texapon MG 1214* deserves particular mention as a foaming agent for tooth pastes and powders as well as foaming mouth washes where it is preferably used because of its very faint taste. *Texapon Extract ASV* is a mixture of special fatty alcohol sulphates. It is particularly suitable for the manufacture of shampoos which are compatible with the mucous membrane of the eyes. *Texapon KM 14 Special* is a mixture of high grade, surface active substances with myristyl alcohol ether sulphate. It is an excellent base for the manufacture of shampoo and bath essences as well as cleansing and rinsing liquids. *Texapon KM 14 Special* is unaffected by hard water and has good compatibility with the skin. *Texapon K 14S Special* is sodium salt of a lauryl alcohol ether sulphate. It is a high grade raw material for the manufacture of shampoos, bubble baths as well as rinsing and cleansing liquids. It is unaffected by water. Due to the fact that the odour of *Texapon K 14S Special* is weak, it can be perfumed easily. Any cloudiness that may occur can be removed without any trouble by a small addition of alcohol. *Texapon MG 12* is magnesium salt of a lauryl alcohol sulphate. Because of its mild taste it is used as a foaming agent for tooth pastes and powders as well as foaming mouth washes. It is also used for making mild and non-irritant emulsion and powder shampoos.

Marchon Products Ltd. offer a wide range of surface-active agents for cosmetics and toilet preparations.

Foaming and wetting agents for dental powders include Empicols LZ, LHC1, MLS, MLSV, LZV and Halvopon MGS. For powder, liquid, cream, lotion and jelly shampoos there are Empicols 2337, MLS, LZ, LM, TLC 20, LQ, TP, TA, SLE, LZV, LMV, L Special, C, TA, MLSV and 1032, Empilans KB 2 and AA 62 and Halvopon PS. Emulsifiers for the manufacture of toilet and cosmetic creams included Empilans 2848 and GMS(SE), Empiwax SK, Laurex 12, 16, 18, CS and NC. Foam stabilisers for shampoos include Empilan AL, CM, LDE and AA 62. Opacifiers for cream and lotion shampoos comprise: Empilans 2848 and GMS and Empiwax SK. Emulsifiers for hand and hair creams include Empilans GMS (SE), KL 2 and KL 6 and Empiwax SK.

Sipon Products Ltd. have also completed the range of synthetic surface-active agents for cosmetic applications. The recent additions are: *Siposan*, which is N-lauryl ethoxylaminosulphonic acid and used in disinfectants or detergent germicides; the incorporation of alkyl chlorides in cationic range; *Sponol O*, which is sodium dioctyl sulphosuccinate and used as a cosmetic wetting agent; *Super Sipon L.230*. *Super Sipon L.230*, although only the triethanolamine salt of sulphonated lauryl alcohol, has an advantage over the conventional products because the unsulphated alcohol is maintained at less than 0.5%.

*Collone QA* (Glovers (Chemicals) Ltd.) is the latest addition to a range of emulsifying agents where cationic emulsions are required. Being positively charged emulsions formed from *Collone QA* adsorb more strongly on the skin and hair or, in

general terms, those surfaces associated with a negative charge, and are thus efficacious where positive adhesion is required.

*Armeen Z* (Armour Hess), N-coco beta amino butyric acid, is an amphoteric surface-active agent. It is a bactericide and fungicide. By virtue of its low degree of colour, odour and toxicity it has many applications in cosmetics. It will not affect the hair or skin in the concentration used, so it is useful for shampoos, face creams, shaving creams and soaps, etc. Ethoduo-meens are N-alkyl trimethylene diamines—ethylene oxide condensation products of Duomeens. They are cationic surface-active agents with two cationic groupings and are used in hair tint preparations, making the hair more receptive to tinting.

*Emulgade A* (Dehydag) is a mixture of higher saturated alcohols, predominantly cetostearyl alcohol, with non-ionic emulsifying agents based on saturated fatty alcohol polyglycol ethers. It is a self-emulsifying base for the manufacture of ointments, creams and oil-in-water liquid emulsions. It is specially suitable for preparations with a high water content and fluid components and is a useful ingredient for countering the effects of components which tend to impair emulsion stability or make emulsification difficult.

*Etolans* (Corda) are non-ionic surface-active agents of an entirely new type in which the lipophilic portion of the molecule is due to mixed sterols (cholesterol), trimethyl sterols (lanosterol) and high molecular weight aliphatic alcohols, as distinct from products based purely on aliphatic alcohols already available. They can be used as emulsifiers and auxiliary emulsifiers

for producing an oil-in-water emulsion as distinct from the water-in-oil emulsion produced by normal wool wax alcohols. They also act as solubilisers, wetting agents, dispersing agents and gelling agents. Products ranging from water-dispersible to water-soluble are available in the five grades offered.

Loramines U.185 and DU.185 (Dutton and Reinisch Ltd.) are new fungicidal and bacteriostatic agents developed to replace halogenated phenols, quaternary compounds, organic sulphur compounds and organic salts of heavy metals which are toxic or damage proliferating skin. Loramine U.185 is undecylenic acid monoalkylolamide and Loramine DU.185 is undecylenic acid dialkylolamide. The first derivative is relatively water insoluble and is a waxy material which is available in powder form suitable for incorporation into creams or powders. The second is freely water-soluble and is supplied as a viscous liquid suitable for incorporation into aqueous systems. These substances are highly effective against fungi infection, such as athlete's foot, as well as the yeast-like fungi associated with dandruff. In addition, the dialkylolamide derivative has surface-active properties which make it interesting as an auxiliary emulsifier and surface-active agent in some formulations; the monoalkylolamide has interesting properties in the formulation of soaps, as it acts as a perfume fixative and preservative.

#### Lanolin products

Westbrook Lanolin Co. is constantly investigating new processing techniques to develop fine grades of lanolin. The three basic grades of Golden Dawn Pharmaceutical Lanolin are recommended for use in cosmetics, pharmaceutical preparations, soaps, etc.

Alcohol-soluble lanolin (Westbrook) is a fraction of pure B.P. lanolin, free from chemical modification or admixture of any other substances. It is completely soluble at room temperature in all proportions in ethanol. It has the normal emulsifying properties of lanolin and possesses the additional property of forming very fine oil-in-water emulsions, almost colloidal in nature. These can be easily prepared by pouring an alcoholic solution into distilled water at room temperature, with gentle stirring, when dispersion occurs instantaneously.

Lanidrol (Esperis S.A.) is a new

condensed product based on Lanocerina, hydrogenated lanolin. It is completely soluble in water and gives a colourless solution up to 50% concentration. It is also soluble in diluted alcohol. Lanidrol is absolutely neutral, odourless, inoxidisable and stable. It is of special interest to manufacturers of cosmetics where blandness, water solubility and lubricity are desired.

Solulan C-24 (American Cholesterol Products, Inc) is a stable, 100% active, water and alcohol soluble form of cholesterol. It was designed to provide a convenient and economical source of cholesterol for all types of topical preparations, including clear aqueous and alcoholic vehicles and emulsions. Solulan C-24 is the 24 mol. ethylene oxide ether of cholesterol (derived from lanolin). It contains approximately 25% pure cholesterol. It can be used in many products, both emulsified and clear. It is an emollient and an auxiliary emulsifier, particularly useful for hair and scalp formulations.

Hartolite (Croda) a more easily handled modification of Hartolan, is a blend of equal parts of modified superfined lanolin alcohols and liquid paraffin B.P. It is primarily a water-in-oil emulsifier, but additionally, it is a source of cholesterol for cosmetic materials and imparts emolliency to these products. Emulsions produced from Hartolite are far more resistant to heat than those produced directly from Hartolan itself. This heat stability is of great importance when there is the possibility that such emulsions may be stored for long periods in store houses and shops. Hartolite can be employed as the basic emulsifier in most creams and pharmaceutical emulsions of the water-in-oil type. It is of particular value in the production of the "universal" or "general purpose" type of skin creams exploited for their skin protective properties. Such creams are useful where the skin is in regular contact with water, providing the properties of "skin food," cold cream and cleansing cream. They are also valuable materials with which to protect the skin against "chapping" from wind and sun-burn.

#### Fatty acid products

Price's (Bromborough) Limited are extending their interests in oleoderivatives manufactured from their traditional fatty acid and alcohol products. Many have present, or potential, applications in

the cosmetic field. They are able to manufacture also a wide range of esters which have hitherto not been available in the U.K., including caprylates, caprates, laurates, myristates, palmitates, stearates, hydroxystearates, oleates, linoleates, linolates, ricinoleates and elaeostearates. Pelargonates and azelates may also be available. For vitaminised preparations (suggested for skin creams, shaving creams, cleansing lotions, lipsticks, hair creams and shampoos), they are able to supply several esters from a high purity (95%) linoleic acid.

Anhydrides (Price's) are an interesting new range of materials. There are early literature references to these materials having similar biological absorption to triglycerides. They are also said to have germicidal properties and may be a worthwhile experimental medium for cosmetic creams, etc. (one example is stearic anhydride).

Fatty acid ethers (e.g. stearyl ether) are known to be moisture repellent and may be useful additives for powders.

Ketones (e.g. stearone, laurone) are reported to be gelling agents for solvents in cream and ointment formulations. They are compatible with waxes, and with solid and liquid fatty acids and, therefore, may be worth investigating in cosmetics.

Ceraphyls (Van Dyn and Co. Inc.) are new materials for use in both cosmetics and pharmaceuticals. They are lubricant and emollient but non-greasy, non-oily, and non-drying. Ceraphyl 28 Cetyl Lactate and Caraphyl 50 Myristyl Lactate produce highly unusual and desirable results in lipsticks, hand creams, body lotions, hair dressings, deodorants and antiperspirants, suntan preparations and ointments. They impart sheen and silkiness to skin and hair. Ceraphyl 28 Cetyl Lactate acts as a plasticiser in hair sprays, deodorant sticks and as a solvent for dyes. Ceraphyl 31 Lauryl Lactate is indicated for use in hair dressings, antiperspirants and deodorants, hand and body lotions and creams, suntan preparations and ointments. It is an excellent solubiliser and plasticiser.

Alkyl myristate (A. Boake, Roberts) is the latest addition to the range of fatty acid esters. It is a virtually colourless and odourless liquid, the viscosity of which is intermediate between that of isopropyl myristate and cosmetic grade mineral oil. It is oily with a "feel" similar to that of some of the vegetable oils

(e.g. olive and almond oils). It spreads easily on the skin and appears to be absorbed to some extent, leaving a residual film which is neither oily nor greasy and which makes the skin smooth and supple. These properties indicate the potential usefulness of alkyl myristate in a wide variety of cosmetic preparations, where it should be considered not merely as a replacement for other oily materials but, in many cases, as the main oily constituent. It is suggested for use in cold creams, skin cleansing preparations, foundation creams, and also in non-aqueous products such as lipsticks and eye make-up.

Cetiol A (Dragoco) is manufactured by esterification of saturated, liquid fatty acids with saturated, liquid fatty alcohols. It is a colourless, clear, practically odourless, oily liquid which does not become rancid. It is akin to the biological skin fats and is non-irritant. It serves as a fatty component for the manufacture of ointments, creams and emulsions as well as for skin oils. Its slight fatty character makes it particularly suitable for day creams and lotions (complexion milk). Furthermore, it is a good superfatting agent for alcoholic hair lotions, shampoos, toilet soap and shaving soap. Cetiol A is particularly suitable for incorporation in aerosol packs.

Iso-adipate (Dragoco) is readily soluble in both alcoholic solutions and in mineral and fatty oils, and in view of its neutral smell, has been used for various purposes: in alcoholic solutions with a fatty effect on hair and skin, particularly in hair washes for dry hair, and as a lubricant for after-shave skin lotions (electric razor types); as a dissolving intermediary and fixative for odors and perfume oils used in oily and alcoholic products; as a solvent for eosines in lipsticks; as a plasticiser in nail-polishes, and as a thickener in foam baths.

A specially refined grade of hexylene glycol (The Distillers Co. Ltd.) is available for cosmetics. It is marketed under the Bisomel trade name and should not be confused with Bisol hexylene glycol, an industrial grade.

Iso-propyl linoleate (A. Boake, Roberts) is of potential interest to the cosmetic chemist and those concerned with dermatological preparations. It spreads readily on the skin and is comparable in this respect with vegetable oils. It

appears to penetrate the epidermis and also enhances the apparent penetration of saturated materials.

Ricinoleic acids and esters supplied by S. and D. (Est. 1783) Chemical Manufacturing Co. Ltd., include grade N ricinoleic acid which is recommended for cosmetics that have a soft, fatty consistency. It can be used also for neutralising alkaline products and emulsifying fatty oils. Puropol EMP emulsifying agent, from the same suppliers, is a ricinoleic ester of complex composition; it is neutral and gives stable emulsions with mineral and fatty oils, waxes, stearine and tallow.

#### Miscellaneous

Purceline and Purceline Oil (Dragoco) are new **preen-gland esters** (from the preen gland grease of ducks) which complement the sebaceous coating of the skin. They are said to aid in combating desiccation of the skin, injury due to wind, weather and sunshine, or chemical or bacterial influences. The grooming and protective properties of preen-gland esters make the skin supple, smooth and soft. They are recommended for creams, lip salves and lipsticks, soaps, skin and hair oils, hair sprays and hair products. They are also useful in aerosol products to prevent blocking of the valve as a result of cold caused by evaporation during atomisation.

Satinex (A. Boake, Roberts) is a fine white **powder**, especially prepared for cosmetics and toilet preparations. It has an excellent colour, is free from objectionable odours, and is superior to magnesium and zinc stearates. With powders incorporating Satinex, the film produced is somewhat opalescent, and powders can be developed with subtle shade tones to give an attractive, natural appearance to the skin, without the dense "overpowdered" look. The addition of Satinex to lipstick formulations has a creaming effect with the lake colours and produces a lipstick which gives a smooth and even film on application.

A product which has certain advantages over aluminium chloride in deodorant and anti-perspirant preparations is **sodium zirconyl lactate** (F. W. Berk and Co. Ltd.). It is supplied as a clear solution of 50% concentration. It can be diluted indefinitely in water and is soluble in ethanol and has a pH around 7. It is not an irritant and is not injurious to fabrics.

Deodorant 8846 (Dragoco) is a

**halogenated biphenol**, effective against Gram-positive and Gram-negative germs as well as against dermal fungi. It prevents body odour without disturbing the biological functions of the sebaceous glands. It is non-irritating.

Shellsol T (Shell Chemical Co. Ltd.) is a high boiling, high-flash aliphatic **hydrocarbon solvent**. It is a clear, water-white liquid composed almost entirely of isoparaffins. It is of interest to the cosmetic industry on account of its very low odour. It is employed in mascara and may also be used in hair sprays and brilliantine.

**Silicone fluid DP 175** (Imperial Chemical Industries Ltd.) contains both methyl and phenyl groups. The presence of phenyl radical is said to give certain advantages over the standard dimethyl silicone fluids for certain applications, including greater heat stability and improved compatibility with other materials. DP 175 is soluble in aliphatic, aromatic and chlorinated hydrocarbons and also in alcohols, ethers, ketones and esters. It is also completely miscible with liquid paraffin, and for these reasons becomes of interest in the manufacture of pharmaceutical and cosmetic products in which it can be readily employed as an ingredient of suntan lotions, hair lacquers, hand creams, etc.

**Plastocrex D.M.H.F. resin** (Rex Campbell and Co. Ltd.) has a number of advantages over shellac and P.V.P. in hair sprays, hair lacquers and hair setting lotions. Apart from its reasonable cost, it is less hygroscopic than P.V.P. It is both alcohol and water-soluble, enabling the formulator to include a percentage of water in the finishing product to lower production costs. It will not dull the hair and being water-soluble can be readily rinsed out with cold or warm water.

**Rona pearl pigments** (natural and non-lead synthetic) (Brown and Forth) are added to cosmetics to produce a pearly iridescent lustre or metallic effect. Principal usage is in nail enamels, lipsticks, eye make-up and hair preparations, and to a lesser extent, in lotions, creams, shampoos and face powders. Rona pearl non-lead synthetic pigment is based upon a bismuth oxychloride product and although not completely light stable it produces a very superior lustre and brilliance. Extensive animal toxicity studies are reported to prove the product to be non-toxic.

## PERFUMERY MATERIALS

### Florals

New specialities have been introduced by Rhone-Poulenc S.A. Angelica R.P. has the peppery fruity tonality of angelica. It gives an original "start" to perfumes in vogue and is suitable for modernising compounds. Arbutone has a powerful odour, faintly "greasy" and waxy (flower wax). This note is found at the end of evaporation in most absolutes. It can be employed as a binder in floral compounds as well as in fancy bouquets and is especially recommended in jasmin, tuberose, wood and Russian leather tones.

Cetojasmin, while being remarkably powerful and tenacious, has a refined note and this greatly facilitates its use both in jasmin perfumes and in fancy compounds, imparting to them a certain individuality. Hyacinth Base R.P. is distinguished by its modern tonality and is a choice element in compounds with a floral note. Narcissus 15, which has a remarkable flowery uplift, gives excellent results in extracts with a modern note. Rhodianyl has a carnation note with warm and persistent background. It is recommended for all carnation, origanum tones, and generally for all floral notes, to which it imparts, at the same time, velvety softness and tenacity.

Rhodialdehyde introduces a modern aldehyde note in perfumes to which it is added but offers the valuable advantage of not imparting the hardness which pure aldehydes give. Tuberose D.P.M. is a base which has a warm note of tuberose flowers. Ylang No. 19 has a distinctive olfactory note. This product introduces a new interesting element. Lavender Intensifier R.P. is a new body which gives a lavender top-note to synthetic lavender or lavandin. Lemon Intensifier R.P. gives added power to lemon compounds. Orange Intensifier R.P. increases the power of orange essences. Pine Intensifier R.P. gives more body and vigour to pine compounds and imparts the balsamic note of pine needles.

International Flavours and Fragrances have introduced some interesting products. Rosalva possesses a unique floral note of good stability and persistence which in small amounts imparts an "aldehyde"

effect, and in quantities up to 2% contributes a distinctive and lovely rose note to a bouquet. Lyral has an odour reminiscent of hydroxy-citronellal but is much more diffusive and persistent. It gives a background floral odour for a wide variety of compositions. Vertinex H.C. has a strong, rich woody note reminiscent of gamma methyl ionone. It exhibits excellent stability in all media, including soap. Vertofix Cœur possesses a very fresh, sweet, diffusive, rich, woody odour. Its musk-like quality is distinctive and adds much to the sweetness of a perfume. This is an exceptionally fine, long-lasting note which has application in all high-grade fragrances. It is similar in character to both vetivert and ionone. Pseudo linalyl acetate has a refreshing bergamot and lavender-like note with a slight nutmeg suggestion. It is far more stable, powerful and flowery in soap than linalyl acetate. Tetrahydro Muguol is a powerful flowery aromatic of wide application, especially suitable in rose and muguet compounds. It has a fresh linalool-like top note, very strong and persistent in soap.

From Haarmann and Reimer comes jasmin 10400A, a pure, well-rounded flower oil of the absolute type which can be used in all compounds without disturbing their harmony. Vertiflor C, an original

bouquet with wonderful freshness and uniformity, is suitable for modern cream perfumes. Fleural C is an interesting novelty with a fascinating, brilliantly fresh bouquet. Due to its extremely pure odour, it may be favourably incorporated in fashionable compounds. Lilac 10315C is an interesting new type, accentuated fresh odour which resembles very well the odour of lilac in full blossom. Lily of the Valley 10340C resembles very well the odour lily-of-the-valley with its cool freshness and pure sweet note. It is equally suitable as a constituent for fancy compounds and as a perfume oil.

Ligustre (Soflor Ltd.) is an exceptionally strong floral base and modifier. Used in small quantities it faithfully reproduces the honey note found in all natural odours. It is stable in soap and non-irritant, but will cause slight discolorations so that for the compound to be used in white products the percentage should not exceed 2-3%.

Vertonal (Soflor Ltd.) is a base and modifier which imparts an intense "green" note akin to the after-rain freshness of prolific growth, or to shelled peas.

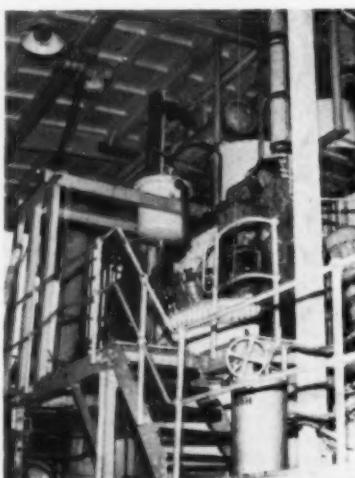
### Synthetics

Folrosia (Givaudan) is a new synthetic aromatic with a deep red rose character and nuances which are reminiscent of the green rose foliage and have a high degree of naturalness and florality.

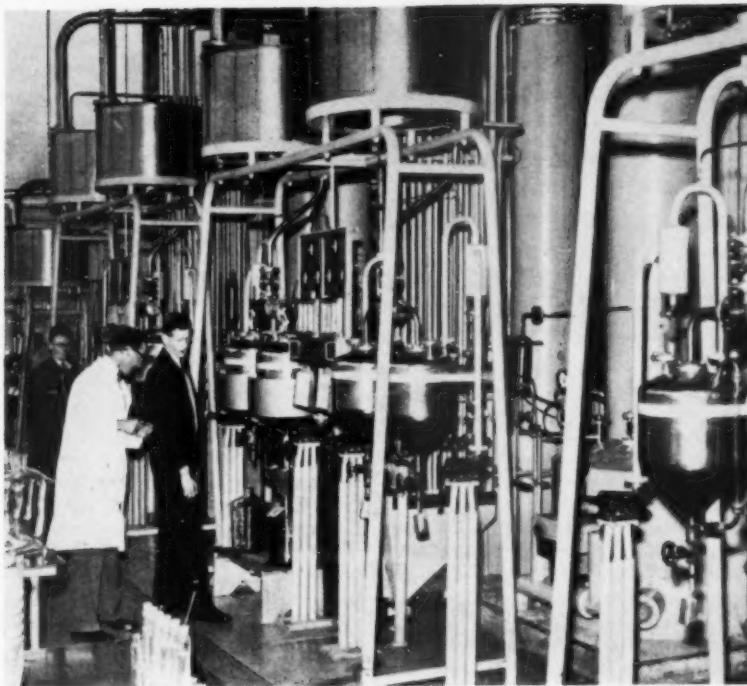
Lactoscatone "Dragoco" is a new aromatic lactone with a typical faecal note. It is the first nitrogen-free aromatic chemical with a fragrance reminiscent of skatole and, therefore, the only chemical in this classification which cannot cause discoloration when mixed with other components. It has a warm animal background accompanied by a delicate woody note and a remarkable fixative power.

Maronyl (Hermann Dullberg) is a new uniform aromatic chemical of extraordinary tenacity and intensity of emanation. It has a warm smell, resembling tropical fruits and the smell of fresh roasted chestnuts. Maronyl gives, especially to floral and fancy compounds, outstanding new top notes and influences by its elasticity and tenacity the whole smell development of the compound, even when used in a very small dosage.

Neodiantol (Hermann Dullberg) is a new aromatic chemical which



Typical reactors used in the manufacture of aromatic perfumery and materials.



**Givaudan and Co. Ltd.'s distillation plant for perfumery chemicals, probably the most modern of its kind in Europe.**

does not alter perfume characteristics but stresses the light carnation note. It is recommended for the construction of top notes, especially in carnation and other floral compounds. Many fancy notes and synthetic essential oils will get an interesting rounding effect and increased tenacity.

Veritone (May and Baker Ltd.) is a new speciality with a rich, sweet odour and an outstanding persistency. It has a number of properties which make it an unusually interesting introduction. It enhances and exalts other odours from an ordinary level to the exquisite and has excellent blending and fixing properties. It is especially useful as a pre-fixing agent for ethyl alcohol and isopropyl alcohol. It is stable in soaps and aerosols as well as in conventional perfumes, is non-toxic and safe for use in cosmetics, perfumes and soaps.

Iso lignyl acetate (du Crocq) is an ester of a terpene alcohol with a woody note. Combined with certain aldehydes, it is an excellent base for modern perfumes.

Drago-Jasimia (Dragoco) is a straight chemical which represents an ester of isomeric octinols. It possesses a radiant and flowery, slightly wax-like note. Its scent and

fixative value resemble those of absolute jasmin pomade. The use of this perfume principle is indicated in a number of compositions—for perfumes, lotions, creams, powders, shampoos, etc., and particularly for soaps as well, as it is stable to alkalies and does not stain.

#### Musks

Musk DTI (Firmenich) is a new indane musk, 1,1-dimethyl-4-acetyl-6-tertiary butyl indane. It combines an intense, very natural, warm and pervasive musk odour with remarkable lasting power, much greater than that of other musks in its category. Its action in a blend is perceptible from the first moments of evaporation onwards in the fullness and "body" it gives to a perfume. It homogenises and rounds off the perfume. It blends basic constituents, oakmoss tones, resinoids, woody and spicy notes, etc. It does not impede the development of the afternotes of flower absolutes, but rather sustains them without overlaying them, leaving all the richness of the flower.

Celestolide (International Flavors and Fragrances) is another trade name for the same indane musk.

Phantolid (Soflor) is a pure chemical which represents a new

structural concept in Tonkin musk synthetics. The odour is similar to that of the principal odour constituents found in natural musk materials. It is a powerful modifier and tenacious fixative. As an ingredient of perfume compounds where a warm musk note is required without the disadvantages of discoloration and poor solubility of the nitro musks or the high costs of the macrocyclic musks, it is particularly useful.

Tonquinolide (du Crocq) is a new product in the range of polycyclic musks, very advantageously priced. Suitable for all sorts of perfumes and for use in soaps.

#### Sandalwood

The very high prevailing price of East-Indian (Mysore) Sandalwood oil is the cause of acute difficulties for consumers, especially soap-makers. Santal R.D. (Roure-Bertrand) was introduced to meet this emergency. It is made up of natural products obtained from woods and other materials of a vegetable origin. It may be used either as such or in conjunction with East-Indian sandalwood oil.

Sandela GD (Givaudan) has recently been introduced as a replacement material for natural sandalwood oil. Sandela GD can be used in perfume formulations in exactly the same manner as sandalwood oil. This new polycyclic alcohol maintains the popular characteristic persistent and tenacious odour of oil of sandalwood, at a price which is less than half that of natural oil.

Santalys LFL (Lautier Fils) is another substitute for sandalwood oil. It possesses the characteristic note of true sandalwood to a very high degree and can be recommended as a very suitable replacement for parts or all of the genuine sandalwood oil.

#### Miscellaneous

For some years, it has been known that the Furocoumarins are the photosensitising agents contained in essential oils. Bergamot oil (Dragoco) is an oil from which the Furocoumarins have been removed by a procedure which does not impair the smell of genuine bergamot. It is an oil from which only the skin-irritants have been removed.

Geranium Body BS (Haarmann and Reimer) is almost a straight chemical body containing traces of other ingredients and possessing the

(Continued on page 511)

# Sulphonation of Detergent Raw Materials with Converter Gas

By Dipl.Chem. A. Davidsohn

*A new converter gas sulphonation process for detergent raw materials has been developed in Israel and is being used in a plant at Dalia in that country. The products are especially suitable for making liquid detergents, solvent-detergents and emulsifying agents. The process is described here by the inventor.\**

THE most important development in sulphonation processes in recent years was the introduction of sulphur trioxide as a sulphonation agent, replacing sulphuric acid, oleum and chlorosulphonic acid in the manufacture of anionic syndets.

After the introduction of liquid  $\text{SO}_3$  a strong impetus was given to the development of sulphonation processes using  $\text{SO}_3$  in a dilute gas stream. In fact, most processes using  $\text{SO}_3$  are using it in the dilute gaseous form. An exception is the process used by the U.S. firm "Pilot" (California), where liquid  $\text{SO}_3$  is diluted in liquefied  $\text{SO}_2$  and this liquid mixture used as the sulphonation agent at very low temperatures (below 0°C.). The  $\text{SO}_2$  is removed as vapour from the reaction mixture and re-liquefied and recycled into the process. The process gives very good results but quite naturally is expensive.

When using liquid  $\text{SO}_3$  in stabilised form the main units of equipment are: (a) Air drying unit with exact measurement of air. (b)  $\text{SO}_3$  dosing and feeding unit. (c)  $\text{SO}_3$  heating unit with the dried air passing through it. (d) Sulphonation unit. These are the bare essentials of the plant. As it is, one also needs special storage tanks for the liquid  $\text{SO}_3$ , well protected against any trace of humidity and kept always at temperatures above the melting point of liquid  $\text{SO}_3$ , i.e. above 16°C. The pipes carrying the liquid  $\text{SO}_3$ , too, must be kept above 16°C. and well protected against humidity. It will easily be understood what trouble it would cause if  $\text{SO}_3$  becomes solidified in the pipes. As is well known,  $\text{SO}_3$  in its undiluted form is extremely reactive and dangerous. Contact with water, and especially organic material, e.g. lubricating oil, may lead to violent explosive reactions with danger to personnel and machinery. Some firms trying to

sulphonate with  $\text{SO}_3$ -gas, but aware of the dangers and difficulties of handling liquid  $\text{SO}_3$ , have tried to obtain the  $\text{SO}_3$  from 60%  $\text{SO}_3$ -oleum, from which the  $\text{SO}_3$  is distilled off in a stream of dry air or in another manner.

Considering that dry-air diluted  $\text{SO}_3$ -gas should not contain more than 10% (per volume) of  $\text{SO}_3$  in order to obtain the best sulphonation results, it appears absurd that first a sulphuric acid plant has to absorb the gas from the converter in sulphuric acid to give high  $\text{SO}_3$ -oleum, then to distil the  $\text{SO}_3$  from the oleum to stabilise the distilled-off  $\text{SO}_3$  so that it has the low melting point of 16°C., and that the detergent factory then has to vaporise this highly dangerous and difficult-to-handle liquid  $\text{SO}_3$  to give a gas stream of less than 10%  $\text{SO}_3$ , which in fact is in its composition very similar to the converter gas that was used to make, by a rather roundabout method, the liquid  $\text{SO}_3$ . As we shall see later on, converter gas does not contain as much oxygen as the air used for vaporising the liquid  $\text{SO}_3$ , so that the composition of converter gas is much better suited for the sulphonation of detergent raw materials. In many countries liquid  $\text{SO}_3$  or 60%  $\text{SO}_3$ -oleum is not available at any price, so it would not be possible to sulphonate with  $\text{SO}_3$ -gas obtained from these materials. The obvious need to find a cheaper and simpler source of  $\text{SO}_3$ -gas induced me to work out a process which gives a controlled  $\text{SO}_3$ -gas stream straight from sulphur.

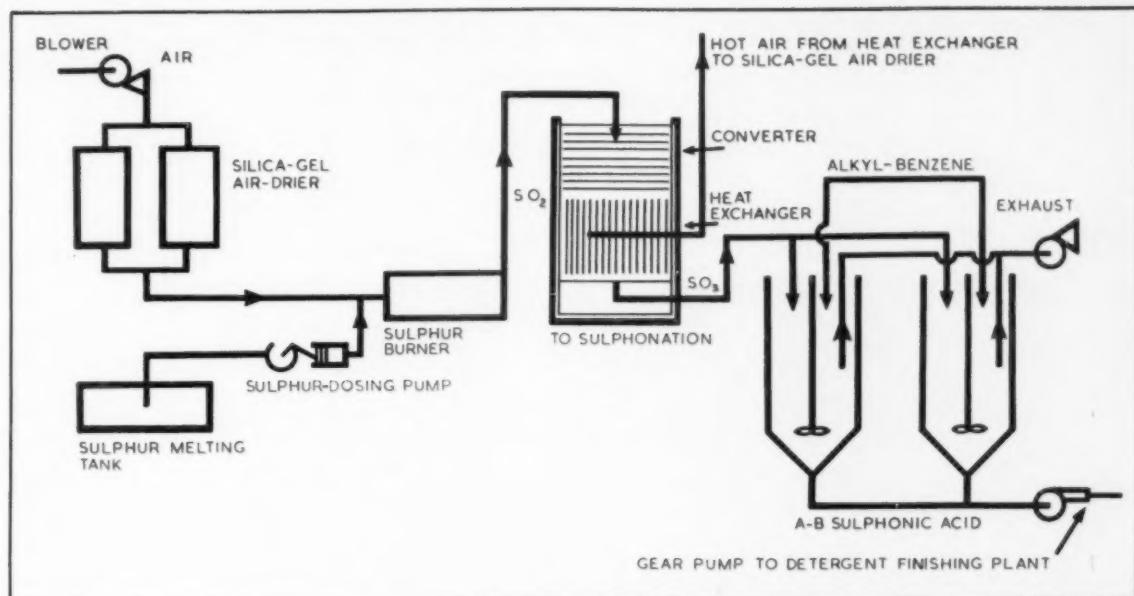
## Direct sulphonation experiments

Experiments have been and are being carried out to sulphonate alkyl-benzene directly with converter gas (with about 7-9%  $\text{SO}_3$ ) from a sulphuric acid plant. Such processes are being carried out in

the U.S., England, Russia, Sweden and probably elsewhere. The disadvantage of such a procedure, namely the splitting off of a converter gas stream from a large converter plant, is evident. First, there is the necessity to have the detergent plant near and dependent on the sulphuric acid plant. Secondly, it is very difficult, if not impossible, to measure the amount of converter gas split from the main gas stream in such an exact manner that good sulphonation results are obtained. In Russia, for example, sulphonation with converter gas was therefore only carried to about 80% of complete sulphonation. I suppose the reason for this limit is the difficulty of exact measurement. Large alkyl-benzene producers in the U.S. are publishing procedures for sulphonation of alkyl-benzene with converter gas. However, as far as I am aware, practical processes have not yet been worked out in the U.S. Recently Marchon in the U.K. and Huels in Germany have marketed converter gas sulphonated alkylbenzene. But there still remains the problem that in such a case the detergent plant has to be closely connected in every respect, locally as well as commercially, with the sulphuric acid plant.

Efforts have been made to overcome the difficulties in sulphonating with converter gas by setting up a specially designed sulphur-burning and converter plant where the total amount of  $\text{SO}_2$ , i.e. the total gas stream from the converter, is used for sulphonation. The underlying idea of this patented process<sup>1</sup> is to measure the  $\text{SO}_3$  used for sulphonation not by measuring the  $\text{SO}_3$  itself but by measuring the amount of sulphur used for producing it. The precondition for such a method is that the sulphur

\* This article is based on a paper read at the 3rd International Congress on Surface Activity, Cologne, September 1960.



Flow diagram for semi-continuous sulphonation process.

used is of high purity, *e.g.* Texas sulphur of 99.5% purity or, better still, gas-sulphur of 99.98% purity, such as the French sulphur now on the market in Europe. The dosing is done by a dosing pump measuring the molten sulphur and pumping it into the small sulphur burner. The air used for burning the sulphur to  $\text{SO}_2$  and converting it in the small converter to  $\text{SO}_3$  is dried by a silica-gel drying unit, bringing the humidity of the air down to a maximum of 0.5 g./cu.m. air. The gas stream leaving the converter has an  $\text{SO}_3$  content of 7.8% and is cooled in a special heat exchanger to a temperature of about 50°-60°C. (The converter gas leaving the converter has a temperature above 400°C.) The heat given up in the heat exchanger may be used as regenerating heating medium for the silica-gel unit (see flow-sheet).

Once the conversion rate of the converter is established (generally 95-97% conversion ratio  $\text{SO}_2/\text{SO}_3$ ) it would mean that each kg. sulphur burnt and transformed into  $\text{SO}_2$  gives *ca.* 2.4 kg.  $\text{SO}_3$ . An additional advantage of the sulphonation process with converter gas over the sulphonation process with  $\text{SO}_3$  from liquid  $\text{SO}_3$  is that in the case of converter gas the oxygen in the carrier gas is much less than in the case of air as a carrier gas for vaporised liquid  $\text{SO}_3$ . This of course is because about half of the

oxygen in the air is used for the transformation of the sulphur to  $\text{SO}_3$ . The relatively small percentage of oxygen in the  $\text{SO}_3$ -gas stream does not cause the unpleasant oxidation side effects so often encountered in the case of air as carrier gas for vaporised  $\text{SO}_3$ . A possible modification of the process is to arrange deliberately for the conversion rate in the converter to be low, *e.g.* 80%. In this case the gas stream for sulphonation would contain a surplus of  $\text{SO}_2$  as reducing agent, thereby giving even lighter coloured AB-sulphonates than is the case with normal conversion rate. However, in this case the conversion rate must of course be a constant one, and a scrubber must be arranged for scrubbing the "tail-gas" leaving the sulphonation set-up. The scrubbing medium is suitably dilute caustic soda, which becomes transformed into sodium bisulphite as a by-product.

Even with the normal conversion rate of more than 95% with no excess  $\text{SO}_2$  in the gas stream one obtains a very positive "deodorisation effect" during the sulphonation process, as all traces of volatile odour-forming substances are carried into the exhaust by the carrier gas stream. Indeed, the AB sulphonates obtained are practically odourless, which is a definite advantage over the conventional acid sulphonation process.

The material balance of the converter gas sulphonation process in comparison to the acid sulphonation and liquid  $\text{SO}_3$  sulphonation process is as follows:

For the sulphonation of

100 kg. alkyl-benzene:

150-160 kg. monohydrate

or 105-110 kg. oleum (20-23%  $\text{SO}_3$ )

or 35-36 kg. liquid  $\text{SO}_3$

or, in the case of the described process,

14-16 kg. sulphur (99.5-99.98% S).

Of course other materials than alkyl-benzene may also be sulphonated by this process, such as fatty alcohols and ethylene oxide adducts.

#### Semi-continuous sulphonation

Now something must be said about the sulphonation process itself as carried out with converter gas from exactly dosed sulphur. In the first production plant employing this process at Dalia (Israel), sulphonation is carried out in a kind of semi-continuous process, namely in two small sulphonating vessels of *ca.* 250 litres. The production unit produces  $\text{SO}_3$  from 500 kg. sulphur/24 hr. This means 1,200 kg. of  $\text{SO}_3$  as converter gas (7.8%  $\text{SO}_3$ ), enough for *ca.* 3,000 kg. alkyl-benzene/24 hr. 175 kg. (200 litres) alkyl-benzene are exactly dosed into

the sulphonation vessels. During the time (ca. 68-70 min.) it takes to sulphonate this amount in one sulphonating vessel, the finished sulphonation mixture in the other one is "aged" for 15 min., a small amount of water is added, and the alkyl-benzene-sulphonic acid either run into storage or immediately transformed into the neutralised AB sulphonate. The small amount of water (ca. 2-3% in the sulphonate mixture) helps to overcome "anhydride sulphonate" formation and keeps the colour of the AB sulphonic acid stable, even on prolonged storage in mild steel drums or tanks. In fact the main "control instrument" on the sulphonation side of the plant is a clock. Of course dosing, timing, filling, etc., may be carried out by automatically controlled valves, etc. On the other hand, it is also possible to transform the process into a fully automatic one by having the alkyl-benzene dosed constantly at the bottom of the sulphonation vessels, where it comes into contact with the  $SO_3$ -gas stream, and to have the sulphonic acid constantly flowing out of the vessel into the aging vessel, etc., by an overflow at the top of the sulphonating vessel (the Ballesta modification of the process).

#### Heat exchange

It is well known that the heat of reaction for sulphonating alkyl-benzene with  $SO_3$  is much greater than with acid or oleum. Thus heat exchange during sulphonation is of great importance. Furthermore, the high viscosity of the reaction mass at the end of the sulphonation makes heat exchange difficult. Therefore the sulphonation vessels are fitted with cooling jacket, cooling coil, and a side-arm heat exchanger, through which the reaction mass is circulated by means of a gear pump. In principle the sulphonation procedure is not different from the one described for the sulphonation with vaporised  $SO_3$ ,<sup>2</sup> so that I will not give more details here. It may only be mentioned that the type of agitator is also of great importance, as well as the proper distribution of the  $SO_3$ -gas stream.

It is important to carry out tests on complete sulphonation on the spot in the shortest possible time. A method was worked out<sup>3</sup> which is based on the fact that a 10% sodium AB sulphonate solution gives turbidity on dilution 1:1 with methanol, in case the percentage of

For 100 kg. detergent raw material	$SO_3$	Sulphur	Yield in kg. 100% active matter (sodium sulphonate)
Alkyl-benzene (AB) .. .. ..	33-35	14-16	140
Lauryl alcohol .. .. ..	40	16-18	150
Ethylene oxide condensate (Octyl-phenol 5 mols ethylene oxide) .. .. ..	19	8-9	123
Xylene .. .. ..	75	33-34	197
Toluene .. .. ..	87	38-39	212

Table 2.

Active detergent matter calculated as the sodium salt of the DDB-sulphonic acid .. .. ..	100% ( $\pm 1\%$ )
Unsulphonated matter calculated on 100% active detergent matter .. .. .. 100 parts of DDB-S 100 need for neutralisation:	1.5% - 2%

13-14 parts caustic soda (NaOH)  
or 47-51 parts triethanolamine  
or 34-37 parts diethanolamine  
or 19-21 parts monoethanolamine.

unsulphonated matter is above 1.5%. This test can be carried out in not more than 2 min. by the plant operator on the spot, and makes it possible to have the sulphonation controlled without having to wait for a time-consuming quantitative test in the laboratory.

A single worker is operating and controlling the  $SO_3$  production unit and the sulphonation unit. By attaching a continuous neutralisation unit to the sulphonation plant, neutralisation as well can be carried out by the same operator.

Table 1 gives the raw material balance and the yield for various detergent raw materials.

A typical specification of AB sulphonic acid obtained by this process is shown in Table 2.

Of course, it is always possible to sulphonate mixtures of many components with converter gas. In fact co-sulphonation of e.g. xylene or toluene together with alkyl-benzene has many advantages, as the final sulphonate is less viscous than is alkyl-benzene alone. The final products obtained by sulphonation with converter gas are especially suitable for the manufacture of all types of liquid syndets, solvent detergents and emulsifying agents, because the sulphonates are practically free of inorganic salts (sodium sulphate).

Even for use in spray-drying towers these modern types of sulphonates are of advantage. Because only traces of uncombined sulphuric acid are present in the acid sulphonate, the sulphonic acid can be neutralised without external cooling; danger of iron pick-up is non-existent. In fact, in the case of AB sulphonic acid it is simpler to prepare the slurry for the spray-

drying (either continuously or discontinuously) from the AB sulphonic acid than from the AB-S-Na paste. The AB sulphonic acid can be fed in the slurry production unit by dosing pumps, which considerably simplifies operations.

#### REFERENCES

1. Israel patent 12,536. (Patents in other countries pending.)
2. E. J. Carlson, G. Flint, E. E. Gilbert and H. R. Nychka, *Ind. Eng. Chem.*, 1958, **50**, 276.
3. A. Davidsohn, *Soap Perfumery Cosmetics*, 1958, **31**, 392.

#### NEW INTEREST IN MEDICINAL PLANTS

(Continued from page 489)

production costs promised to be low, the Institute recommended the trial cultivation of pyrethrum. From these trials the area under cultivation increased to such an extent that in 1939 Kenya superseded Japan as the world's largest pyrethrum producer, and this crop is now a substantial dollar earner and East Africa's third largest export.

An achievement such as this cannot be expected often. Indeed, where medicinal plants are concerned, one may search for many years and fail to find the "wonder drug" which, at heart, is the hope of most workers in this field. However, the search is always worth while, and when the aim is not solely to discover an outstanding substance new to medicine but also to establish new and improved sources of known drugs, thus aiding the economy of a territory poor in natural resources, the chances of success are considerably increased.

# New Lighting Code Sets Higher Standards

By D. E. Greenhalgh\*

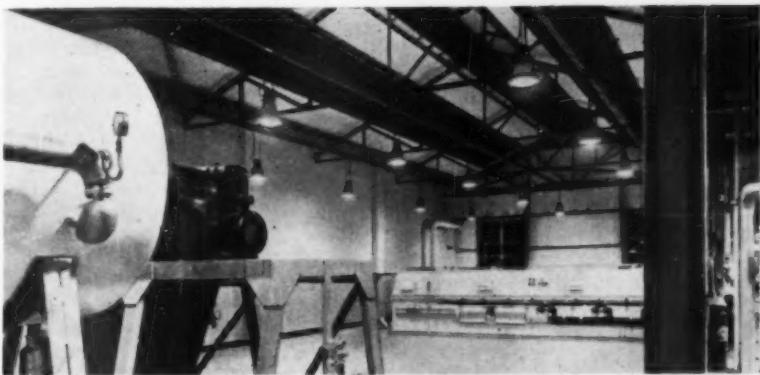
*The pharmaceutical and chemical industries have special requirements for lighting in factories and laboratories, so for them a new code of lighting in buildings has added interest. Recommendations are made for both artificial and natural lighting.*

TWENTY-FIVE years ago the Illuminating Engineering Society published a guide to good interior lighting in buildings. During the war, when the beneficial effect of good lighting upon industrial production was of national importance, the Society re-issued the work, revised and enlarged, as its first "Code for Lighting in Buildings."

Since then and through several editions, it has remained the standard work of reference on the illumination requirements of a vast range of interiors. While it has always been familiar to lighting engineers, the Code is now also becoming well known to architects, works electricians and far-sighted managements.

1961 will be remembered in the field of illuminating engineering as the year in which the new Code was published; for although the current edition continues to recommend the level of illumination needed in many working areas, it additionally introduces two important related matters. Firstly, a new method for assessing direct discomfort glare from artificial light sources has been developed, and the Code gives limiting values of glare index for most illumination recommendations. Secondly, the Code examines the question of daylight design and the allied concept of permanent supplementary artificial lighting.

Clearly then the new Code will greatly interest those in the pharmaceutical and fine chemical industries, certain sections of which are well known for their specialised lighting requirements. Laboratories and packaging areas, for instance, usually call for quite high levels of illumination. As a rule such high levels must be obtained partly by artificial means because daylight penetration into most buildings—excepting those with glass roofs—is surprisingly poor. Certain other working areas within the industry, although not necessarily needing high levels of illumination, do require special fittings suitable for operation in



200 watt flameproof pendants light this drying section in a Welsh chemical plant to about 20 lm./sq. ft. The substantially regular arrangement of fittings would permit numerical assessment of the possible glare from an installation of this kind.

moisture-laden, corrosive or explosive atmospheres.†

## Illumination levels

Recommended levels of illumination on the working plane have been raised in the new Code and are in line with good current techniques and present economic conditions. In the manufacture of pharmaceuticals such processes as grinding, granulating, mixing and drying, and tabletting, should be lighted to at least 30 lumens per sq. ft. A similar level should be regarded as a strict minimum in all inspection areas where the visual task is often difficult, and considerably higher illuminations are often justifiable provided that glare limits are observed. Plant processing and fine chemical finishing call for levels of 20 and 30 lm./sq. ft. respectively. Areas in which raw materials are stored require about 20 lm./sq. ft.

Although the above are recommendations for special processes, the Code caters for the general case. It explains quite simply a method for calculating the minimum illumination requirement for any visual

\* British Lighting Council.

† I.E.S. Technical Report No. 1. Lighting in Corrosive, Flammable and Explosive Situations.

task in terms of apparent size and maximum reflection factor of critical detail within that task.

## Glare

Well-designed lighting fittings, suitably installed, put enough light where it is wanted—on the working area—and prevent it being wasted where it is not wanted; light in the wrong direction is always wasted and nearly always causes trouble. Glare may be broadly defined as a condition produced by too great a proportion of light entering the eye from the wrong direction. No matter what kind of work is being done, the object of regard should always be the brightest thing in the field of view. If this is not so, distraction occurs and, depending on the relative size, brightness and position of its source, the distraction may be uncomfortable or even disabling.

Glare may be caused by a direct view of a light source (which might be a lighting fitting or a window), indirectly by the reflected image of the source in a specular surface near the line of sight—perhaps a polished bench or desk top—or by large variations of brightness within the normal field of view. The last mentioned is often the result of the contrast between the brightness of

a light source and its darker background, but may be sometimes caused by violent colour variations in a decorative scheme. When glare is present in an interior its effect is nearly always uncomfortable rather than disabling. Glare is not always immediately obvious, but the irritation and discomfort it causes grow with time. Indeed, when a management receives complaints from its staff that "there is something wrong with the new lighting" the reason is nearly sure to be discomfort glare.

The new Code tackles the problem of discomfort glare by developing the work of the Building Research Station who first evolved an expression for measuring it numerically. A number of factors are involved, including room dimensions, reflection factors of room surfaces, mounting height and orientation of fittings and the manner in which they distribute light. Clearly a fitting which concentrates light downwards and upwards will not cause much direct glare when the normal line of sight is roughly horizontal, but on the other hand a diffusing fitting which emits a good deal of light sideways towards the observer may be much more troublesome, especially in a large room where there are many such fittings.

#### Discomfort assessment

Assessment of glare may be made for any lighting system, but most easily for general lighting where the arrangement of fittings is substantially regular; fortunately this covers the majority of installations.

When the above-mentioned data have been applied to the glare tables in the Code a glare index for that particular installation will be obtained. Reference to the Limiting Glare Index for the process involved (which appears in the schedule in Part 3 of the Code) will indicate whether or not the installation is too glaring. If its glare index numerically exceeds the recommended limit the design should be modified by using lighter coloured decorations, or raising (or perhaps reorienting) the fittings, or even by selecting fittings having a more appropriate light distribution for the room in question. Limiting values of glare index have been most carefully selected and strict observation of them is essential if an installation is to be satisfactorily comfortable.

In the pharmaceutical and fine chemical industries the areas most

likely to be affected by limiting glare indices are those where close work is done—laboratories, for example. Laboratories have a limiting index of 19, while most other areas within the industry for which comparable illumination levels are recommended have a limit of 25. Packaging departments need good lighting and some of them, usually in pharmaceutical concerns, also require sterile conditions. The use of lighting fittings mounted flush with the ceiling is then necessary. However, this type gives no upward light and tends to produce a dark ceiling which emphasises the brightness of the fitting—a clearly undesirable condition. Fortunately the problem can be largely solved by using light-coloured, non-glossy decorative finishes on room and working surfaces.

#### Flameproof fittings

The use of flameproof lighting fittings is essential in some parts of the industry. When such areas are indoors and need a general lighting system a certain glare limit will be applicable. In order to give the most efficient distribution of what light is available from the necessarily restricted lamp wattage, flameproof fittings often use optical systems. These have the two-fold advantage of giving more light on the working plane while also reducing direct glare. The use of flameproof fittings with clear well glasses containing bare lamps will usually cause severe glare when used in general lighting schemes, although their simplicity may be advantageous in certain other applications.

The last part of the Code is devoted to aspects of daylighting design and permanent supplementary artificial lighting. While the daylighting of buildings is the realm of the architect rather than the illuminating engineer the above-mentioned aspects are so closely related that it is appropriate to discuss them here together.

#### Daylighting and P.S.A.L.

Daylight enters a building by roof lights or side windows, or sometimes by both. In either case supplementing and eventual substitution is necessary as daylight fades. The north light roof which for many years was widely used is now recognised as an expensive way of lighting an interior. Nowadays an adequate level of electric lighting can be installed and operated for

less cost than the provision and maintenance of roof daylighting, bearing in mind the cost of heat lost this way during the winter. The concept of windowless buildings, although generally unpopular with employees, is actually used in at least one plant in the pharmaceutical industry. The lighting, although totally artificial, is of generous level for the processes involved and in this case the operatives are quite happy.

Most modern industrial buildings are naturally lighted by side windows which do, of course, possess the advantage of enabling employees to see what is going on outside. Probably the majority of buildings housing the pharmaceutical and fine chemicals industries are of this type. However, unless side windows are unusually large they are quite incapable of adequately lighting more than just the areas near them. Moreover, if side windows are of such size they also begin to suffer some of the shortcomings of roof lights and in any case are dependent on weather conditions and time of day; and if they are the only light sources in daytime they may also be sources of considerable daylight glare.

The best compromise for a room which is fairly deep to the back wall and is lighted from one side only appears to be a combination of moderately sized "amenity" windows and permanent supplementary artificial lighting of the far side of the room. This arrangement if suitably designed, has the advantage of illuminating the whole area suitably and sufficiently while retaining the impression of natural lighting. The level of illumination produced by a permanent supplementary scheme must be related to the level of outdoor daylight rather than to the requirements of particular visual tasks and therefore quite often exceeds them. Thus we have the rather unusual situation of being able to turn *down* the lights (at the back of the room) as soon as daylight fails, so as to make the whole room evenly lighted by the normal artificial lighting system.

In this brief survey of the new I.E.S. Code it has been possible to pick out only the salient points, but a thorough perusal of it by managements is recommended, for it clearly shows that *if properly designed* a lighting installation can now do everything required of it, and often better than daylight.

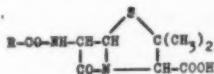
## Antibiotics

By A. N. Boyd,\* M.A.

“Synthetic” penicillins · Acid-stable penicillins · Penicillinase-stable penicillin · Broad-spectrum penicillin · Paromomycin · Kanamycin · Antibiotics and the common cold · Anti-tumour antibiotics, Actinomycin D · Mitomycin C · Streptonigrin

### “SYNTHETIC” PENICILLINS

THE penicillins have the following general formula:



The most widely used penicillin is penicillin G (benzylpenicillin, R = C<sub>6</sub>H<sub>5</sub>—CH<sub>2</sub>) which is produced when phenylacetic acid is added to *Penicillium chrysogenum* fermentations. It is used extensively in treating diseases caused by Gram-positive bacteria. It has however certain disadvantages, such as: acid instability, which means that it cannot be given orally; susceptibility to destruction (and hence inactivation) by penicillinase, so that it cannot be used against penicillinase-producing bacteria; and low activity against most Gram-negative bacteria.

In 1953, K. Kato<sup>1</sup> suggested that the penicillin nucleus (in which R—CO is replaced by H) is present in *P. chrysogenum* fermentations to which no side-chain precursor has been added. Total synthesis of the nucleus (6-amino penicillanic acid) was achieved by J. C. Sheehan,<sup>2</sup> but it involved many stages and the yields were not high. Its production has, however, been made practicable by F. R. Batchelor *et al.*<sup>3</sup> who have shown that it can be isolated in crystalline form from *P. chrysogenum* fermentations to which no precursor has been added. The nucleus itself is biologically inactive. The discovery of 6-amino penicillanic acid has made possible the preparation of many “synthetic” penicillins and this has helped in the search for

penicillins without the disadvantages of penicillin G. These “synthetic” penicillins can be made by acylating the penicillin nucleus with suitable acid chlorides.

### Acid-stable penicillins

Penicillin V (phenoxyethyl penicillin, R = C<sub>6</sub>H<sub>5</sub>—O—CH<sub>2</sub>) is not a “synthetic” penicillin but is produced when phenoxyacetic acid is added to *P. chrysogenum* fermentations. It is much more stable to acids than is penicillin G and can therefore be taken orally. A further advance was made by E. T. Knudsen and G. N. Rolinson<sup>4</sup> who prepared phenethicillin (*α*-phenoxyethyl penicillin, R = C<sub>6</sub>H<sub>5</sub>—O—CH—CH<sub>3</sub>) from 6-amino penicillanic acid. The proprietary name of phenethicillin is *Broxil*. Phenethicillin is acid-stable and has the advantage that it is absorbed much more rapidly than penicillin V, giving blood levels two to three times as high. It is slightly more stable to staphylococcal penicillinase than penicillin G is, but slightly less active against other bacteria.<sup>5</sup>

### Penicillinase-stable penicillin

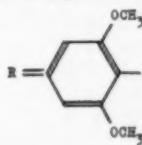
In September 1960, G. N. Rolinson *et al.*<sup>6</sup> announced the preparation from 6-amino penicillanic acid of a new penicillin, methicillin (2 : 6-dimethoxyphenylpenicillin, the pro-

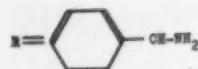
prietary name for which is *Celbenin*. This substance was found to be resistant to staphylococcal penicillinase and more stable to penicillinase produced by *Bacillus cereus* than is penicillin G, even though it induces the formation of the enzyme. It competitively inhibits the inactivation of penicillin G by *B. cereus* penicillinase but not the inactivation by staphylococcal penicillinase. Methicillin can be used against staphylococcal infections resistant to penicillin G, though it is only about one-fiftieth as active against penicillin-sensitive staphylococci. It is also absorbed and excreted rapidly and therefore frequent injections of high doses are needed. Early work<sup>6</sup> showed that although cultures of *Staphylococcus pyogenes* became tolerant to methicillin *in vitro*, this did not occur *in vivo* and no naturally occurring resistant strains could be found. More recently, G. T. Stewart<sup>7</sup> has shown that, *in vitro*, strains of *S. aureus* showed a limited capacity to develop resistance and *S. albus* quickly acquired a high degree of resistance. However, and this is more important, when strains were re-isolated from methicillin-treated patients, *S. albus* showed a low degree of resistance and *S. aureus* showed none, even when isolated from patients treated with low doses of methicillin for up to eight weeks, a situation that would normally favour the emergence of resistant strains. The resistant strains of both *S. aureus* and *S. albus* did not completely inactivate methicillin and this suggests that resistance to methicillin depends on mechanisms different from those involved in resistance to penicillin G. One naturally occurring resistant strain of *S. aureus* has been discovered by M. P. Jevons<sup>8</sup> in patients who have had no contact with methicillin, but it is important to note that there was only one naturally resistant strain among 5,440 strains examined. Unlike phenethicillin, methicillin is not acid-stable and therefore must be administered by injection.

### Broad-spectrum penicillin

The most recent penicillin prepared from 6-amino penicillanic acid is ampicillin D(-)-*α*-aminophenyl-

\* Glaxo Laboratories Ltd.





Penbritin.

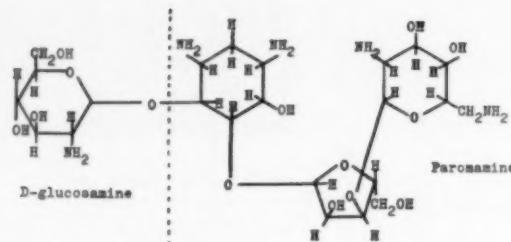
penicillin,<sup>9</sup> the proprietary name of which is *Penbritin*. Its activity against sensitive staphylococci, haemolytic streptococci and pneumococci is similar to that of penicillin G. Like penicillin G, it is attacked by the penicillinase of resistant staphylococci. Unlike other penicillins, it is active against many Gram-negative bacteria: *Salmonella*, *Shigella*, *Escherichia coli* and some species of *Proteus*. Other *Proteus* species, *Klebsiella aerogenes* and *Pseudomonas pyocyannea* are, however, much more resistant either intrinsically or because they produce penicillinase. Unlike the broad-spectrum antibiotics chloramphenicol and tetracycline, ampicillin is bactericidal. It is also non-toxic and, being acid-stable, may be given orally.

The three main disadvantages of penicillin G have therefore largely been overcome by the development of the three "synthetic" penicillins, pheneticillin, methicillin and ampicillin, the last being both an acid-stable and a broad-spectrum antibiotic. Time will show whether all three defects can be rectified in a single penicillin of high potency.

#### PAROMOMYCIN—AN AMOEVICIDAL ANTIBIOTIC

Paromomycin is an antibiotic discovered in fermentations with a Streptomyces resembling *S. rimosus*. This Streptomyces was obtained from a soil sample collected in Columbia<sup>10</sup> and is now known as *S. rimosus* forma *paromomycinus*. The trade name for paromomycin is *Humatin*.

Paromomycin is extracted from fermentation broth as follows:<sup>11</sup> Filtered broth is adjusted to pH 7.2 and the antibiotic is absorbed on to resin by passing the broth down a column of a sodium-form carboxylic resin, e.g. Amberlite IRC-50. After the rich resin has been washed with water, the antibiotic is eluted with 0.5 N hydrochloric acid and the eluate is adjusted to pH 9.5. The eluate is stirred for 30 minutes with a mixture of filter aid and activated charcoal that absorbs the paromomycin. Paromomycin is eluted from the charcoal with 0.1 N sulphuric acid. The eluate is passed through a hydroxyl-form anion-exchange resin to adjust the pH to 9.0 and the



Suggested structure of paromomycin

effluent from this column contains the free base. Paromomycin may be obtained in solid form as the free base, the sulphate or the hydrochloride by freeze-drying a solution of the base or the appropriate salt.

T. H. Haskell, J. C. French and Q. R. Bartz<sup>12</sup> have suggested that paromomycin is a glycoside of D-glucosamine with the structure shown above.

The most commonly used salt of paromomycin is the sulphate, a white, stable, water-soluble, amorphous powder. Paromomycin is a potent, broad-spectrum antibiotic, active *in vitro* against Gram-positive, Gram-negative and acid-fast bacteria including the human tubercle bacillus,<sup>10</sup> and it is effective *in vivo* against *Salmonella* and *Shigella* species.<sup>11</sup> It is also active *in vitro* against many fungi, including three that are pathogenic for man, viz. *Phialophora pedrosoi*, *P. verrucosa* and *Actinomyces bovis*.<sup>10</sup> The antibiotic showed no antiviral activity in tests that included poliovirus, adenovirus, herpes simplex virus and measles virus, even at the highest doses non-toxic for the cell cultures.<sup>10</sup> Paromomycin shows marked anti-protozoal activity *in vitro* and its most important property is its directly amoebicidal action against *Entamoeba histolytica*, the protozoan parasite that causes amoebic dysentery. Clinically, paromomycin is extremely effective in the treatment of intestinal amoebiasis<sup>13</sup> and it has also cured enteric infections by *Shigella sonnei*, *Salmonella paratyphi B* and *S. typhimurium*.<sup>14</sup>

Paromomycin has a very low oral toxicity, but parenterally in high or prolonged dosages it may cause renal damage, which, however, is reversible when treatment is stopped. The antibiotic is only poorly absorbed by the bowel. This possibly explains its low toxicity, but it means that it cannot be used orally against systemic infections.

Paromomycin is unique among antibiotics as it is the only one so far

discovered that is non-toxic, directly amoebicidal and able to be used effectively against amoebiasis.

#### KANAMYCIN

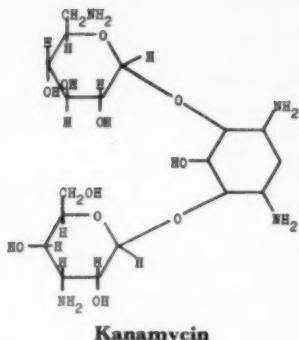
Kanamycin was discovered by H. Umezawa *et al.*<sup>15</sup> in fermentations with a Streptomyces isolated from a soil sample collected at the Nagano Prefecture in Japan. The Streptomyces was subsequently named *Streptomyces kanamyceticus*. The proprietary name for kanamycin is *Kannasyn*.

Broth fermented with *S. kanamyceticus* contains two antibiotics. One is active against both *Bacillus subtilis* and *Mycobacterium 607* and can be absorbed by cation-exchange resins but cannot be extracted by butanol. The other is active only against *B. subtilis* and cannot be absorbed by cation-exchange resins, but it can be extracted by butanol. The former is predominant and is called kanamycin.

Kanamycin is absorbed by passing broth through a sodium-form cation-exchange resin column, e.g. Amberlite IRC-50. After being washed with water, the column is eluted with 0.5 N hydrochloric acid. The pH is adjusted to 6.0 and the solution freeze-dried. The solid is dissolved in methanol, and after filtration acetone is added to give a white precipitate. Repetition of the resin process gives a product with a potency of 400 to 500 µg./mg. Kanamycin is further purified by the preparation and recrystallisation of the reineckeate which can readily be converted to other salts, solutions of which can be freeze-dried to give pure solid substances.

Kanamycin hydrochloride is soluble in water and methanol, and slightly soluble in ethanol, but it is insoluble in other organic solvents. The sulphate is soluble in water but not in any organic solvents.

M. J. Cron *et al.*<sup>16</sup> have suggested the following structure for kanamycin:



Kanamycin and neomycin have identical antibacterial activity *in vitro*, and there is complete cross-resistance of organisms to both antibiotics. Kanamycin is active against most strains of staphylococci encountered clinically, but resistance to it can be induced among sensitive staphylococci as with penicillin. Because it is only slightly absorbed from the gastro-intestinal tract, the drug must be given parenterally for systemic infections.

Unfortunately, kanamycin is rather toxic, with effects similar to those of neomycin and streptomycin and, as in the case of dihydrostreptomycin, it can cause irreversible deafness. Because of this, the antibiotic should be reserved for serious systemic infections by staphylococci resistant to safer drugs and for those urinary-tract infections for which it is the only effective antibiotic. It should not be given to patients with impaired renal function, as in such cases deafness might occur after treatment has been stopped.

#### ANTIBIOTICS AND THE COMMON COLD

The common cold is believed to be the result of a virus infection. Much work has been done to find a cure for it, but so far no successful treatment has been discovered. J. M. Ritchie<sup>17</sup> has suggested that bacteria normally present in the nasopharynx invade the tissues during the course of the virus infection and aggravate the effects. He has further suggested that the symptoms during the first few days are caused by the virus itself and afterwards by the secondary bacterial infection. This hypothesis was supported by a successful clinical trial<sup>18</sup> in which autogenous vaccines or small doses of antibiotics were administered at the beginning of the cold to prevent secondary invasion by bacteria.

A further trial has been carried

out by C. B. McKerrow, P. D. Oldham and S. Thomson<sup>19</sup> (a) to see if treatment with antibiotics would prevent aggravation of bronchitis in subjects with pneumoconiosis who often assert that an attack of bronchitis succeeds a head cold; and (b) to try to confirm and extend J. M. Ritchie's findings in normal subjects. Members of a group of patients with colds were given either dummy lozenges or lozenges of tetracycline, oxytetracycline or chlorotetracycline, according to the sensitivity of their salivary flora. After four days the state of the cold was assessed as "cured," "better but not cured" or "unchanged." Disappearance of the cold was regarded as success, better or unchanged colds were regarded as failures.

Results were similar for the bronchitic and normal subjects. Overall 23% of the colds were "cured" in three days by dummy lozenges and 50% by active lozenges, a significant increase. After the trial, more subjects had resistant salivary organisms than before. Although these were also found in those given dummy lozenges, it is important that the question of the development of drug-resistant organisms should be investigated before antibiotics are used on a large scale for treating the common cold. There were some instances of tongue and throat soreness among patients treated with chlorotetracycline and oxytetracycline. J. M. Ritchie also noticed this<sup>18</sup> and suggested simultaneous treatment with vitamins.

The results of this trial suggest that, although it may not be possible to treat the common cold itself with antibiotics, it may be possible to hasten its recovery by preventing secondary bacterial infection, provided that drug-resistance does not develop.

#### ANTI-TUMOUR ANTIBIOTICS

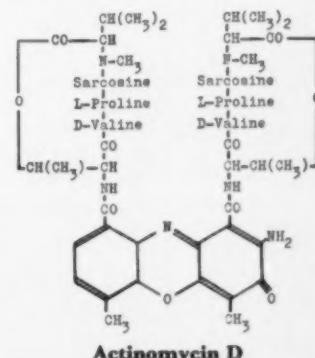
In recent years there has been much investigation, particularly in Japan, into the production of anti-tumour antibiotics. There have been many reports of antibiotics active against experimental tumours, though claims for cures in man are rare. Anti-tumour agents can be detected by adaptations of the mammalian cell assay described by H. Eagle and G. Foley.<sup>20</sup> The chromatographic assay using monolayer mammalian cell cultures under an agar overlay is a useful method for screening fermentation broths. When

such an assay shows that a broth contains an active substance, the antibiotic may be extracted and tested in animals such as mice, rats and hamsters bearing transplants of small tumours. Tumours commonly used include forms of the Ehrlich carcinoma, adenocarcinoma, Lewis carcinoma, leukaemia, Crocker carcinoma and human tumours. Three anti-tumour antibiotics that have aroused considerable interest recently are actinomycin D, mitomycin C and streptonigrin.

#### Actinomycin D

Actinomycin D is produced in fermentations with *Streptomyces parvullus* in a tryptone/starch/dextrose medium.<sup>21</sup> Whole broth is adjusted to pH 5.0 with hydrochloric acid. It is then stirred for 30 minutes with Darco G60 or Norit A charcoal and the antibiotic-rich charcoal is filtered off. The cake is washed with water followed by 60% acetone and actinomycin D is eluted from the charcoal by acetone or ethyl acetate followed by benzene. After evaporation of the solvents a solution of the crude antibiotic in benzene is applied to a column of silicic acid. The column is washed with 20% ethyl acetate: 80% benzene to remove impurities and the actinomycin D is eluted with ethyl acetate. Evaporation yields relatively pure actinomycin D which can be further purified by recrystallisation from absolute ethanol. Actinomycin D can also be obtained by solvent extraction with butanol.

Actinomycin D is a bright red crystalline solid melting at 241–243°C. It is optically active and has an absorption spectrum typical of the actinomycins. Its structure has been elucidated by E. Bullock and A. W. Johnson:<sup>22</sup>



In doses of 0.025 to 0.05 mg./Kg., actinomycin D has been shown<sup>23</sup> to

be active against both the solid and ascites forms of the Ehrlich carcinoma and it completely inhibited the growth of Krebs 2 carcinoma and ascites carcinoma 180. Actinomycin D is also active against human tumours H.S. No. 1 and H.Ep No. 3 implanted in suitably prepared female rats.<sup>24</sup> There was 89% inhibition of H.S. No. 1 by 0.06 mg./Kg. intraperitoneally and 40% inhibition of H.Ep No. 3 by 0.03 mg./Kg.

In a clinical trial, 67 patients with advanced cancer were treated with actinomycin D.<sup>25</sup> Twelve patients showed a dramatic but transitory regression. The treatment caused nausea and vomiting, severe ulceration of the mouth and tongue, and in a few cases alopecia, acne, pharyngitis and diarrhoea.

Some work has been done on the mechanism of the action of actinomycin D against bacteria. G. E. Foley used *Lactobacillus* strains and suggested<sup>26</sup> that the antibiotic interferes with pantothenic acid-dependent reactions concerned with the biosynthesis and/or utilisation of amino acids, but I. J. Slotnick<sup>27</sup> was unable to confirm this with *Bacillus subtilis*. Further work by I. J. Slotnick<sup>28</sup> indicated that inhibition of *B. subtilis* is bacteriostatic and that at inhibitory concentrations the antibiotic suppresses the assimilation of ammonia and completely inhibits the formation of certain inducible enzymes by *B. subtilis*. This supports G. E. Foley's view<sup>26</sup> that actinomycin D interferes at some point in reactions involved in the biosynthesis of cellular protein.

### Mitomycin C

An antibiotic complex, mitomycin, produced by a new Streptomyce called *Streptomyces cespitosus*, was first described by R. Sugawara and T. Hata.<sup>29</sup>

The complex was separated into six fractions by Wakaki *et al.*<sup>30</sup> using a complicated procedure. The complex was absorbed from fermentation broth by carbon and eluted with acetone. The acetone solution was concentrated, hydrated and then extracted with chloroform. The aqueous layer yielded a red powder. The chloroform extract was passed down an alumina column, and white crystals were recovered from the effluent. Eleven coloured bands were observed on the column which was cut into layers, the latter being eluted with methanol. Four fractions were recovered: reddish crystals

(mitomycin A), violet crystals (mitomycin B), yellow crystals and bluish-violet crystals (mitomycin C).

Mitomycin C does not decompose at temperatures up to 360°C. It has been given the tentative molecular formula  $C_{34}H_{61}N_{13}O_{19}$ . Reactions indicate that it contains double bonds and amine, phenol and ketone groups. It is soluble in water, methanol, acetone, butyl acetate and cyclohexanone, slightly soluble in benzene, carbon tetrachloride and ether, and insoluble in light petroleum. It is unstable in acid or alkaline solutions; organic solutions are inactivated by visible light.<sup>30</sup>

The antibiotic has strong anti-tumour activity against the Ehrlich ascites carcinoma in mice in doses of 40 to 1,000  $\mu$ g./Kg./day. Its LD<sub>50</sub> was found to be 5,000  $\mu$ g./Kg. intravenously and 9,000  $\mu$ g./Kg. intraperitoneally. It has a peculiar toxicity in mice, causing death from 2 to 14 days after injection. When the biological activity of mitomycin C is lost through boiling its solution the toxicity also disappears.<sup>30</sup>

Beneficial clinical trials have been carried out by N. Shimada *et al.*<sup>31</sup> and K. Sukie *et al.*<sup>32</sup> and later more extended trials have been carried out by Y. Shiraha *et al.*<sup>33,34</sup> These workers have reported<sup>34</sup> remarkable improvements in 74 cases out of 194 patients treated, particularly when the antibiotic was given intrarterially. Improvements included regression of tumour (complete disappearance in one case); gain in appetite and body weight; alleviation, and even complete relief, of pain; alleviation of nausea and vomiting and mitigation of cough. Prophylactic use of mitomycin C is also described by Y. Shiraha *et al.*<sup>34</sup> Patients who had had either complete or partial radical surgery for malignant lesions were treated prophylactically with mitomycin C with the aim of preventing a relapse or spread of the malignancy to a previously unaffected part. So far, too few patients have been observed for too short a time to evaluate long-term prophylactic treatment, but the results were promising enough to justify further trials.

Some toxic effects were noticed,<sup>33</sup> the chief of which was leukopenia (fall in the leucocyte count), but withdrawal of the drug usually restored the count within three weeks. There were a few other side-effects such as anorexia, fever, general fatigue and subcutaneous bleeding, but it was difficult to be

sure whether the antibiotic or the disease was responsible.

### Streptonigrin

Streptonigrin is the most recent of the anti-tumour antibiotics. It was reported by W. S. Marsh, A. L. Garretson and E. M. Wesel<sup>35</sup> and is produced in fermentations with certain strains of *Streptomyces flocculus*. Streptonigrin is extracted from filtered broth by *n*-butanol or ethyl acetate at pH 3.0 to 5.0. The solution is concentrated, extracted into buffer and extracted again into ethyl acetate at pH 4.0. Further concentration gives a crude product as a coffee-brown powder. This can be purified by countercurrent distribution and extraction from the appropriate fractions by ethyl acetate or chloroform at pH 4.0, followed by crystallisation first from ethyl acetate and then from acetone or dioxane.

Streptonigrin is a coffee-brown to almost black powder. It decomposes at 275°C., is slightly soluble in water, the lower alcohols, ethyl acetate and chloroform, and is more soluble in dioxane, pyridine and dimethyl formamide. The empirical formula of streptonigrin is  $C_{24}H_{20-22}O_8N_4$ . It behaves as a weak acid with quinonoid properties.

The antibiotic is active against a broad spectrum of bacteria including *Micrococcus*, *Bacillus*, *Mycobacterium*, *Salmonella*, *Klebsiella* and *Pseudomonas* species. The anti-tumour activity of streptonigrin has been investigated by J. J. Oleson *et al.*<sup>36</sup> who have shown that for transplants in mice it is very effective against carcinoma 775 and human tumour H.S. No. 1, moderately effective against sarcoma 180 and L1210 leukaemia and slightly active against human tumour H.Ep No. 3, though W. S. Marsh *et al.*,<sup>37</sup> M. N. Teller *et al.*<sup>38</sup> and P. C. Merker *et al.*<sup>39</sup> report significant inhibition of transplanted H.Ep No. 3.

Streptonigrin is a very toxic substance given parenterally, causing 25 times as much bone marrow depression as mitomycin C, and also leukopenia, thrombocytopenia (decrease in number of blood platelets), diarrhoea, anorexia and loss of weight,<sup>40</sup> though its oral toxicity is much lower.<sup>36</sup> Thus, although streptonigrin is a very powerful anti-tumour antibiotic, its high toxicity will severely restrict its use in cancer therapy.

Research into anti-tumour antibiotics is proceeding rapidly. Tests

(Continued on page 514)

# Pest Control Chemicals

By D. P. Hopkins, B.Sc., F.R.I.C.

*Effects on food flavour · Scottish research · Vegetable weedkillers · Clubroot and calomel · Spray formulation · Carbamate insecticides · Earthworm control · Spray chemicals for fruit*

## Effects on food flavour

THE broader aspects of flavour or taste in foods have been discussed in the recent Agricultural Research Council's annual report<sup>1</sup>—modern methods of both cropping and food processing have "caught the agriculturist and food scientist unprepared because it has never hitherto been thought worth while to spend much effort on the understanding of the tastes and flavours of our everyday foods, or on the methods of analysing and evaluating them." However, some U.S. papers were published at about the same time and these report fairly sizeable and long-term efforts to assess effects of pest control chemicals upon crop flavours. The major of these papers<sup>2</sup> reports a six-year experiment by seven experiment stations and the U.S.D.A. Bureau of Human Nutrition to measure these effects upon 20 vegetables and three fruits. Organoleptic panel methods of flavour testing were employed; but panels varied from 5 to 40 or more trained people. The specific results are so innumerable that they cannot be summarised here. They include 528 evaluations on 36 single insecticides, 152 on 18 combinations of insecticides; 66 on 11 single fungicides, and 118 on 11 combinations of fungicides. However, some broad conclusions have been drawn even though they must be regarded as tentative for this quantity of evidence is insufficient to eliminate the flavour effects of other influences, known and unknown.

The single insecticides which in general did not induce measurable declines in flavour or off-tastes were: chlordane, DDT, Dibrom, Dilan, dimethoate, heptachlor, phosphamidon, Sevin, Thiodan and Trithion. Off-flavours were found with BHC, lindane and toxaphene in 21, 10 and 20% of samples respectively. Five single insecticides seemed more notable for off-flavour induction:

BHC, lindane, toxaphene, endrin and malathion. Some insecticides seemed more adversely influential when used in combinations than when used singly; these were toxaphene, Sevin and malathion. There were some cases of improved flavour, e.g. 10 to 13% of samples treated with chlordane, heptachlor, lindane and endrin. This reflects the complexity of the problem since some of these insecticides are among those also scoring adverse effects. In no case did a sample treated with insecticide combinations show improved flavour.

Fungicides were tested less in this work and on a smaller range of crop products. Three single fungicides, Bordeaux mixture, tribasic copper and zineb, showed no ill effects on flavour and induced better flavour in a third of the tests. PCNB showed ill effects for most samples. Fungicides used in combination did not in general induce off-flavour, but in combination with insecticides captan and thiram were more suspect than others. Much of the fungicide testing work was limited to one crop, potatoes.

Another somewhat similar U.S. study<sup>3</sup> has dealt with weedkiller effects on crop flavours. Crops for canning were mainly involved and 28 different weedkillers were tested. Taste panel assessments found that 11 of the weedkillers reduced flavour in the processed product, 17 did not. Anglo-interpretation of these results in detail is not helped by the fact that commercial names for the weedkillers are used and the scientific names for active constituents are not also given in all cases; the products were used at manufacturers' recommended rates, but in some cases excess rates were also tested. The favourable group of 17 included: atrazine, CIPC or chloro-IPC, dalapon, endothal, EPTC, monuron, natrin, DNPB, salt, trietazine. In the less favourable group of 11 were:

chlorazine, diuron, neburon, CDAA, simazine and 2,4-D. It must be pointed out, however, that the tasting panels in this work with weedkillers were composed of highly-trained tasters and some of the adverse flavour effects found might not also be detected by an ordinary consumer panel. Also, none of the sample scores for flavour decline was sufficiently low to make the product unacceptable. Indeed, it seems a reasonable conclusion that modern organic weedkillers when used at correct rates are unlikely to induce notable off-flavouring effects. In the broadest terms the chance of off-flavour development through use of modern pest control chemicals is in the descending order: insecticides, fungicides, weedkillers.

## Scottish research

A recent report from the North of Scotland College of Agriculture<sup>4</sup> contains some interesting test results. Simazine and dalapon have been tested for weed control with raspberries. Simazine applied in late March controlled annual weeds, reduced vigour and growth with perennials. Dalapon plus Simazine was better for this controlled couch grass as well as annual weeds, but unless applied in October-November it adversely affected raspberry cane growth, and application in April-September was ineffective for weed control. Dalapon seems to require more careful timing to avoid some adverse effects on the canes. The same report discusses glasshouse tests with tomatoes for new soil fumigants: methan sodium, mylone, D.D., tridipan and 20% methylisothiocyanate. In 1960 all these gave better tomato yields per plant than the control (no-fumigant) and also than the formaldehyde-treated plot. No off-flavours could be detected for any fumigant treatment. The new fumigants tested are not yet listed in the Agricultural Chemical Approved Scheme. The best yields in 1960 tests were given after the methan sodium and the 20% methylisothiocyanate treatments.

## Weedkillers

Another new report<sup>5</sup> particularly provides information about new weedkillers used for control of weeds in vegetable cropping. Good commercial results were obtained with dinoseb as a pre-emergent weedkiller with French and runner beans. Simazine was successful in weed control in established asparagus

beds. Propazine was an effective pre-emergent weedkiller with carrots and parsnips; trietazine is promising with peas, broad and French beans, field beans. 1960 test results with amiben (3-amino-2,5-dichlorobenzoic acid) on carrots, parsnips and beans suggest a need for further research to ascertain risks to crops. A useful range of weeds could be killed with three new products from U.S., *Karsil*, *Solan* and *Dicryl*, all chlorophenyl amides. Crops showing marked tolerance were carrots, parsnips and parsley. Further work with these weedkillers is to be carried out.

The cost of crop sprays on farms, which mainly involves selective weed-killers, has been examined<sup>8</sup> and costed farms in the Midlands show that between 1953-55 and 1958-60 average farm expenditure on crop sprays has more than doubled. This increase is a feature common to all types of farms, though in the period concerned the increase was more marked for small-acreage farms. This latter finding probably reflects belated appreciation of crop spraying on small farms, not greater use of spraying as a technique. However, crop spraying amounts to an average of only 0.7% of total farm costs; about 1% for arable farms, 0.7% for mixed farms and 0.2% for livestock farms. This examination of the extent of spraying by costs conceals the true size of expansion because costs of the most-used spray materials, e.g. MCPA, have fallen heavily since the mid-1950s.

#### Clubroot and calomel

Sometimes old methods are well vindicated by modern research. Two recently reported investigations have confirmed the superiority of calomel for controlling club root disease. In the first<sup>7</sup> winter cauliflowers were given these comparative treatments: aldrin (0.6%) spot treatment, pure calomel root dip, mercuric chloride solution spot treatment, hydrated lime spot treatment, heavy liming of soil before planting. All treatments were better for yield than the control, but the calomel treatment produced the best yield, 366 crates per acre compared with 344 for mercuric chloride, 223 for aldrin and 220 for hydrated lime. The mercuric chloride treatment, though no doubt as good as calomel in terms of yield, for the small difference can hardly be significant, is less practicable in commercial growing than the calomel dip pre-planting treatment. In the other experiments<sup>8</sup> root dips made

of suspensions of calomel and aldrin were tried with summer cabbage, but there was no increase in control of clubroot for the additions of aldrin with or without a sticking agent in the dip. Thus, calomel as one of the older pest control chemicals remains unchallenged in its best-known field; and it is perhaps not irrelevant to add that modern research has also given it the new field of moss control in turf.

#### Formulation

Stability of malathion in dust formulations is a recognised problem and a new paper<sup>9</sup> suggests that the diluents which cause the least decomposition are those of lower absorptive capacity. Unfortunately these diluents give products of poor flowability and generally poorer application properties. Various glycols were investigated as stabilising agents. A 7% diethylene glycol could change the surface acidity of attapulgite from less than 0.8 to 3.3, but it could not completely eliminate malathion decomposition. This semi-failure prompted further study of the causes of decomposition and it was postulated that alkaline sites on the clay surface (possibly due to calcium or magnesium) were mainly responsible for malathion hydrolysis. Many additives were tested for ability to interact with alkaline surface sites and tall oil compounds showed high promise. The best stabilisers found were two distilled tall oils, *Indusoil M-28* and *Acintol D*; and a distilled tall oil fatty acid, *Acintol FA2*. But, like the glycols, these tall oil products could not entirely prevent malathion decomposition.

The addition of surface-active substances to selective weedkiller sprays has been re-examined in a U.S. paper, so far seen only in a summarised account.<sup>10</sup> At dilute and sub-lethal herbicide concentrations a surface-active additive increased, suppressed or did not affect the herbicide's own activity; this was found for some 80 different additives. Any measurable effect was proportional to the additive's concentration. At high herbicide spray concentrations the surface-active substance's effect could be modified, synergistically or simply additively if the surface-active substance had inherent phytotoxicity. Some of the additives would increase activity for some plants but not for others, e.g. they could increase phytotoxicity towards a legume plant but not towards a cereal. A single surface-active addi-

tive did not always behave similarly when added to the various weed-killers examined. These differences are the basis of a suggestion that sprays might be formulated, using surface-active additives, to meet specific weed-crop situations.

#### The carbamates

The carbamate insecticides, of which Sevin is the best known so far, have been reviewed in a U.S. paper<sup>11</sup> made additionally welcome by its good list of literature references. A point made that is not perhaps widely known is that this class of insecticide is synthetically related to the natural alkaloid, physostigmine, of the Calabar bean. This alkaloid has long been used in medicine for its cholinergic action. In the 1920s synthetic carbamates of similar cholinergic action were made, but they failed later as insecticides because the quaternary ammonium grouping they all contained could not penetrate the insect lipid nerve sheath. This difficulty was overcome in the 1950s when it was found that uncharged molecules spatially similar to the highly charged physostigmine molecule could have a high insecticidal activity. The commercial development of Sevin followed swiftly. New carbamate insecticides being tested are *meta-isopropylphenyl N-methylcarbamate*; apart from a wide range of toxicity to larvae, aphids, beetles, it has greater activity than DDT, aldrin or malathion against adult mosquito flies, but it is not highly active against house flies. It has a higher mammalian toxicity than Sevin. *Meta-sec-butylphenyl N-methylcarbamate* is very similar in level and range of activity but is lower in mammalian toxicity. *4-dimethylamino-3,5-xylyl N-methylcarbamate*, or Zectran, is another carbamate with a wide range of insect control and some systemic activity, and it has a low dermal and mammalian toxicity. Insect resistance to the carbamates has been shown to be possible, but an important discovery is that the carbamates can be synergised with piperonyl butoxide, sulphoxide, octachlorodipropyl ether and several other substances. The activity of Sevin to houseflies can be synergised as much as 30 times. Another paper on this subject<sup>12</sup> puts forward the view that formulating carbamates with synergists will ultimately be of value in reducing the development of insect resistance.

### A new worm-killer

The earthworm is not a pest in most soils, though whether its much-vaunted activities are beneficial to fertility is nowadays debatable. On sports or ornamental lawn turf, however, worms are in the pest class—their casts in spring and autumn severely handicap mowing, although at these times efficient mowing is often most important. It is also highly probable that worms in turf contribute to the spread of weed seeds. Worm control is not cheap and not always as effective as is hoped. Mowrah meal is a traditional wormkiller, but a high rate of application is needed and the worms die on the surface, necessitating much clearance work. Derris can be as effective and less cumbersome, but derris formulations for plant pests are low in rotenone content for this special use on turf. Lead arsenate has been much used, but it is a toxic substance for use on areas that are often open to animals, etc. A new turf wormkiller on the British market<sup>13</sup> is based on chlordane, which is claimed to be a proven wormkiller and is also toxic to leather-jackets and grub pests. It is formulated as a highly concentrated spray or in a solid and granular form. The worms die underground and the toxic effect lasts in the soil for a considerable time. Test evidence for chlordane's toxicity to earthworms has not been noted in the literature, but this may be an omission of reading; if the claims for this new product are justified in use, this could be a useful break-through in controlling one of turf's most troublesome pests.

### Long Ashton research

As usual the annual report from Long Ashton contains numerous papers on pest control research. A valuable review-paper<sup>14</sup> deals with modern spray chemicals used by fruit-growers and the hazards that can arise through mishandling. The confusion among growers caused by the indiscriminate usage of proprietary, common and scientific names is emphasised. The hazard of mercury residues from organomercury sprays or from mercuric chloride is dealt with in a separate paper.<sup>15</sup> Official recommendations define conditions of application as limiting residues of mercury to 0.1 p.p.m. for fruit at harvest time; this must be compared with higher maxima for arsenic of 1 p.p.m. and

for lead of 2 p.p.m. Investigations have shown that from phenylmercuric acetate sprays mercury passes into the fruits by translocation from the leaves. It is not clear from this work, however, whether in commercial spraying mercury residues on or in fruit would be as high, for the experimental procedure aggravated the residue hazard. The same paper has an association with Rosewarne work discussed earlier here;<sup>7</sup> carrots were grown on soil treated (a) with mercuric chloride and (b) with calomel; the carrots with the (a) treatment contained 0.05 p.p.m. of mercury, those treated with calomel were not contaminated.

It is shown<sup>16</sup> that good control of apple aphids cannot be obtained by modern small-volume sprays with pyrethrum, DDT, DDT/BHC mixtures or malathion. Spraying at the green cluster stage requires large-volume application plus a spreading additive, as the aphids are in a well-protected position between the closely packed flower buds. The systemic demeton-methyl can overcome this and malathion, if used in concentrated spray form, can also do this by diffusion through the flower truss tissues. Control of the blackcurrant gall mite has been investigated<sup>17</sup> and it seems clear that the existent method, lime-sulphur spraying, remains the best; a range of systemic insecticides, including schradan, failed to give promise of control, whereas low-concentration lime-sulphur sprays (1% or  $\frac{1}{2}\%$ ) gave good control without apparent damage to the bushes. However, it seems necessary to give several sprays of the dilute lime-sulphur in preference to single sprays of stronger lime-sulphur formulations. The single sprays give less control and incur greater risks of plant damage.

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### COSMETIC AND PERFUMERY RAW MATERIALS REVIEW

(Continued from page 499)

typical geranium character. This product is stable in soap and can be used to advantage in combination with the geranium oil and also for building up synthetic geranium oils.

Three excellent synthetic terpeneless lemon oils (Cocker Chemical Co. Ltd.) are available: Citranova Lemon C.C., Citranova Lemon Fine and Citranova Lemon Fine X. They are based on the best Sicilian lemon oil. Physically and chemically they resemble commercial terpeneless oils but are superior, since none of the essential volatile components is missing, as is the case with many de-terpened oils derived from natural sources. They are entirely satisfactory in all applications when such oils are used at present, including soft drinks, general confectionery, perfumery and the preparation of lemon essences.

Decolorised absolutes, concretes and resinoids are obtained now by improved special process (V. Mane Fils). These decolorised products possess the whole of the odoriferous elements contained in the corresponding colourised materials.

**Bulk Deliveries by Berk**, is the title of the first of a series of booklets published by F. W. Berk and Co. Ltd., Stratford, London, E.15. It deals with hydrochloric acid and certain metal chloride solutions and gives information on installation of bulk storage facilities for these chemicals.

Advice is given on the design, positioning and maintenance of storage tanks, on the materials recommended for use, and on the ancillary equipment necessary for safe and trouble-free operation. Delivery procedures, safety precautions and the prevention of atmospheric contamination are discussed.

# HORMONES and Related Compounds

By R. M. Evans,\* D.Sc. F.R.I.C.

Structural analysis of polypeptide hormones • Cortisone modifications  
New anti-inflammatory steroid • Bioluminescence

## Analysis of polypeptide hormones

AS NOTED in previous reviews, the synthesis of peptide hormones and the biological testing of analogous polypeptides (with alternative arrangements of the component amino acids) continues apace. Meanwhile, new techniques to expedite determination of the structures of these compounds are being further developed. The structure of polypeptides is usually determined by chemical or enzymatic degradation to yield the component amino acids, which are commonly identified by paper chromatography or by separation on ion-exchange columns. The rapidly developing technique of gas-liquid chromatography has now been successfully applied to the separation and identification of amino acids. Johnson, Scott and Meister<sup>1</sup> have shown that the easily formed iso-butyl, *n*-butyl, iso-amyl and *n*-amyl esters of N-acetyl amino acids can be readily and rapidly separated on columns of Chromosorb W coated with polyethylene-glycol. Over 30 amino acids have been successfully separated and identified, only 2 hr. being required for preparation of the derivatives and completion of the chromatographic analysis.

The N-acetyl esters are prepared by reacting the amino acid with the appropriate alcohol in the presence of hydrogen bromide, and the resulting esters are treated with acetic anhydride to yield the required derivatives. The success of the results achieved is indicated clearly by Fig. 1 (reproduced by permission of *Analytical Chemistry*), which illustrates the separation and identification of a mixture containing 14 common amino acids.

Further development is required before this method can be used for the complete analysis of protein

\* Glaxo Laboratories Ltd.

and polypeptide hydrolysates, but preliminary tests show that the yields of the desired derivatives from a wide range of amino acids are almost constant. There is therefore every indication that the technique will serve eventually to determine qualitatively and quantitatively the components of complex polypeptides.

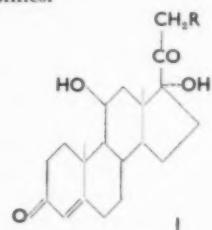
## Analogues of cortisone

Modifications to the structure of the cortisone molecule by introduction of additional substituents or unsaturated linkages have already resulted in the discovery of more active analogues, of which several show diminished adverse side-effects.

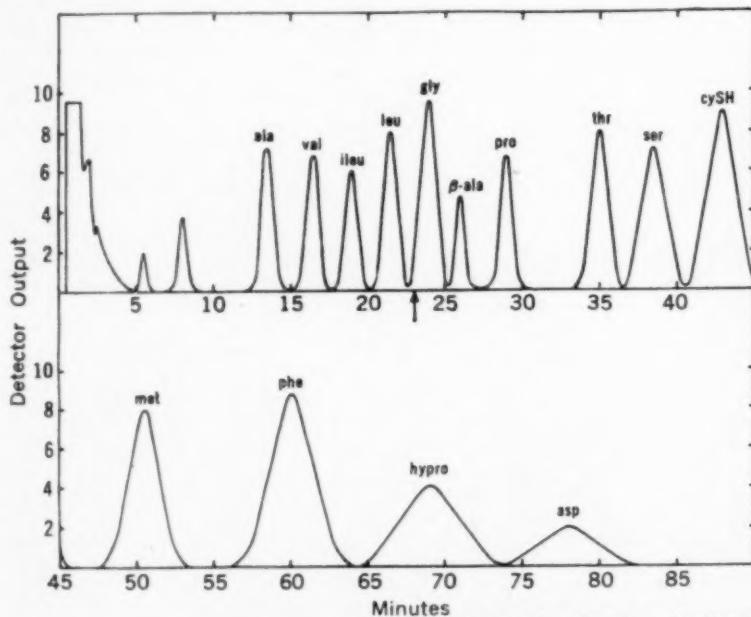
Some of these compounds are now in widespread clinical use; the relation between their structures and activities has been discussed in earlier articles in this series.<sup>2</sup>

No new corticoids possessing outstandingly advantageous properties have been described during the current year, but work in the field continues steadily. Among the structural variants described recently are a series of derivatives of 21-deoxy corticoids and the introduction of 9 $\alpha$ -methyl and 1 $\alpha$ -cyano groups into a range of steroid hormones.

**21-Deoxy-analogues.** Hydrocortisone (I; R = OH) and the corresponding 9 $\alpha$ -fluoro steroid have been converted by Schaub and Weiss<sup>3</sup> into the 21-tosyl esters, which reacted readily with a range of nucleophiles.



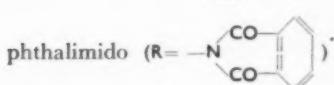
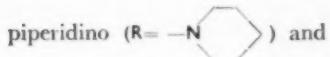
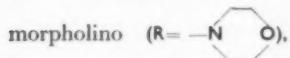
By these reactions the thioacetyl (R =  $-\text{SOC}(\text{CH}_3)_2$ ), mercapto



(From *Analytical Chemistry*, 1961, 33, 671)

Fig. 1. Separation of 14 N-acetylamino acid *n*-amyl esters on an 8 ft. column packed with Chromosorb W, coated with 1% Carbowax 1540. Flow rate, 60 ml. per min.; starting temperature, 125°C.; after 23 minutes (see arrow), temperature was abruptly increased to 148°C.

(R = —SH), methyl mercapto (R = —S.CH<sub>3</sub>),



derivatives were prepared. Similar derivatives of progesterone were also prepared, but, consistently with the findings of previous workers, replacement of the hydroxyl group at 21 served invariably to diminish hormonal activity.

**9a-Methyl hydrocortisone and prednisolone.** There has been much speculation about the reasons underlying the marked effect of 9a-substituents on the biological activities of 11 $\beta$ -hydroxy corticoids. The chemical reactivity of the 11 $\beta$ -hydroxyl group will obviously be affected by both the steric and electronic characteristics of the adjacent group or atom. Opinions have differed on the relative importance of these two factors.

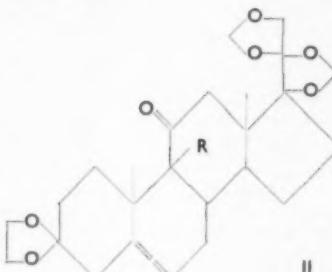
Fried and Bohrman,<sup>4</sup> after a thorough analysis of the evidence, showed that the liver glycogen activities of 9a-fluoro, chloro, bromo, iodo or methoxyl substituted hydrocortisones were enhanced as the electronegativity (as determined by the dissociation constants of the corresponding  $\alpha$ -substituted acetic acids) of the 9a-substituent increased. The bulk of the 9a-substituent appeared to have much less effect, and it was concluded that variation in the acidity of the 11 $\beta$ -hydroxyl group was the dominant factor.

To test further the validity of this hypothesis, Beyler, Hoffman, Sarrett and Tishler<sup>5</sup> have recently synthesised 9a-methyl hydrocortisone (III) and its  $\Delta^1$  analogue (9a-methyl prednisolone). These compounds are of particular interest because the bulk of the methyl group is roughly equivalent to that of a chlorine atom, whereas the acidity constants of propionic and chloroacetic acids differ considerably.

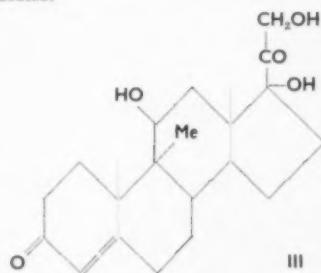
Acid	Acidity constant
ClCH <sub>2</sub> COOH	144 $\times 10^{-6}$
CH <sub>3</sub> COOH	1.75 $\times 10^{-6}$
CH <sub>3</sub> CH <sub>2</sub> COOH	1.34 $\times 10^{-6}$

Jones, Meakins and Stephenson<sup>6</sup> had already introduced 9a-methyl

substituents into simple  $\Delta^7$ -11-keto steroids under forcing conditions, using methyl iodide in the presence of potassium *tert.* butoxide, but these reagents failed with the suitably protected cortisone derivative (II; R = H).



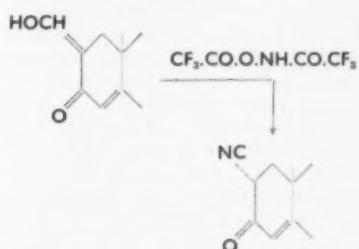
Several alternative methods, including attempted Wagner-Meerwein rearrangements of 11-methyl analogues and the reaction of Grignard reagents and lithium methyl with 9a,11 $\beta$ -epoxides, were tried without success. Methylation was achieved finally by reacting the 9a-bromo-11-ketone (II; R = Br) with methyl magnesium iodide. The 9a-methyl ketone (II; R = CH<sub>3</sub>) was then reduced by lithium aluminium hydride, and the protecting groups were removed to give 9a-methyl hydrocortisone (III), which was readily dehydrogenated by selenium dioxide to 9a-methyl prednisolone.



Liver glycogen assays of these two compounds showed them to have about one-tenth of the activity of the parent corticoids, whereas the activities of the corresponding 9a-chloro derivatives are *ca.* 4-5 times greater. These results provide further confirmation for Fried and Bohrman's hypothesis that the electronic effect of the 9a-substituent is more important than its steric effect.

**1a-Cyanosteroids.** Corticoid analogues of a new series, having a nitrile substituent in position 1, have been synthesised recently by

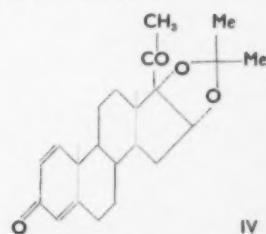
Kissman, Hoffman and Weiss<sup>7</sup> by reacting 2-hydroxy methylene steroids<sup>8</sup> (the 20-keto group having been protected as the ethylene ketal) with O,N-bis (trifluoro-acetyl) hydroxylamine in refluxing benzene. The reaction proceeds efficiently, and examination of the molecular rotation of the products indicates that the cyano group has the  $\alpha$ -configuration.



Biological assessments of these compounds and similar derivatives of the sex hormones are not yet complete, but they have so far shown no outstanding endocrinological activities.

#### New anti-inflammatory steroid

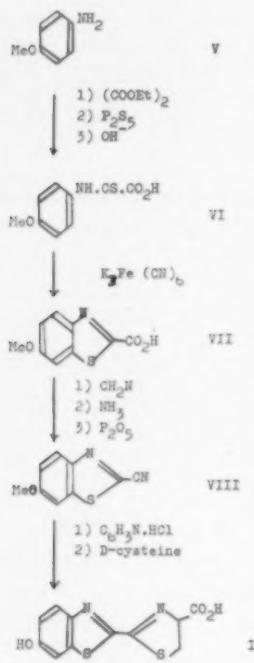
During a search for highly active progestogens, Petrow and his co-workers<sup>9</sup> found unexpectedly that, in the granuloma pouch test, 16a,17a-isopropylidenedioxy-6a-methyl pregn-4-ene-3,20-dione had substantial anti-inflammatory activity. They demonstrated further that, as in the corticoids, this characteristic was greatly enhanced by introduction of an additional double-bond in the 1,2 position (IV).



In preliminary tests on human volunteers, (IV) has shown topical anti-inflammatory activity equal to that of hydrocortisone, thus indicating that the activity is an inherent property of this compound and not due to an oxygenated metabolite. The properties of this compound are particularly interesting, as it is the first steroid lacking an oxygen function at 11 and 21 to show appreciable anti-inflammatory activity.

## Firefly luciferin

From ancient times the phenomenon of the light emitted by the ubiquitous firefly has excited attention and speculation. It has been shown<sup>10</sup> that their light emission involves the interaction of magnesium ions, oxygen, adenosine triphosphate (ATP), the enzyme luciferase and luciferin. The basis of the process is excitation of the luciferin molecules, causing them to emit quanta of yellow light at a wavelength of 550 m $\mu$ . Bydegradative and spectroscopic studies White, McCapra, Field and McElroy<sup>11</sup> have now proved that luciferin has the structure represented by (IX). The structure was confirmed by synthesis according to the accompanying reaction scheme.



*p*-Anisidine (V) was reacted with diethyl oxalate to give the amide, which on treatment with phosphorus pentasulphide and alkaline hydrolysis gave the thio-acid (VI). Cyclisation by potassium ferricyanide to the benzothiazole (VII) was succeeded by esterification with diazomethane, conversion into the amide by ammonia and dehydration by phosphorus pentoxide to the nitrile (VIII). This was demethylated with pyridine hydrochloride. The resulting phenolic nitrile reacted with D-cysteine in

aqueous methanol to give luciferin (IX), identical with the natural material in physical constants and exhibiting the same *in vitro* enzymatic production of light.

In contrast, the analogous compound synthesised from *L*-cysteine was enzymatically inactive.

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## ANTIBIOTICS

(Continued from page 508)

of some of them in animals have been very successful, but there has only been limited success in humans. The relative success achieved with actinomycin D, mitomycin C and streptonigrin will no doubt greatly encourage those engaged in cancer research, and the development of low toxicity antibiotics active against cancer in humans will be eagerly awaited.

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**Hose Book.** W. H. Willcox and Co. Ltd., of Southwark, London, supply hoses for every purpose. A new catalogue lists and illustrates the wide range of Willcox hoses and also covers other hose fittings.

# American Commentary

NEWS AND VIEWS OF THE U.S. PHARMACEUTICAL INDUSTRY by Dr. Rudolf Seiden

*Labelling regulations ★ Safe flavours ★ Physicians' samples abused ★ Antibiotic side-effects  
Insulin shock treatment ★ Foreign drug restrictions*

## Labelling hazardous substances

THE FDA has announced the final regulations of the Federal Hazardous Substance Labelling Act which becomes effective February 1, 1962.

The law requires consumer-protective labelling on common household aids such as bleaches, cleaning agents, detergents, polishes, solvents, waxes and wood finishes if there is a hazard in their use or storage around the house.

The regulation states that the following substances are hazardous because of their toxicity and the frequency of their involvement in accidental ingestion:

1. *Carbon tetrachloride* and mixtures containing it.
2. *Diethylene glycol*, including mixtures containing 10% or more (by weight) of it.
3. *Ethylene glycol* including mixtures containing 10% or more of it.
4. *Petroleum distillates* such as kerosene, mineral seal oil, naphtha, gasoline, benzine, mineral spirits, paint thinner, Stoddard solvent and related petroleum distillates and mixtures containing 10% or more of such products.
5. *Methyl alcohol* including mixtures containing 4% or more of it.
6. *Turpentine*, including gum turpentine, gum spirits of turpentine, steam-distilled wood turpentine, sulphate wood turpentine, destructively distilled wood turpentine, and mixtures containing 10% or more of them.

For some of these substances one or more of the signal words "Danger" and/or "Poison" (and the skull and crossbones symbol) are necessary; all hazardous substances require also proper Warnings or Cautions.

The signal word and the statement of the principal hazard(s) must be placed together on the main panel with instructions to read carefully the other cautionary information elsewhere on the package.

## Safe flavours

A list of flavouring ingredients

determined to be "Generally Recognised As Safe" ("GRAS") under conditions of intended use has been published. The list, issued by the Flavouring Extract Manufacturers Association (FEMA), was compiled by a panel of experts selected by the FEMA. In addition to the 662 ingredients on the list, 130 others are being evaluated further.

## Physicians' samples misused

The FDA discovered recently that repackaged physicians' samples were being sold in some retail pharmacies, instead of being used by physicians in their professional practices.

The Commissioner of the FDA recommends a reduction in the distribution of physicians' samples of drugs; a system of accounting for drug samples; the destruction by physicians of samples they do not use; and a practice of not using physicians' samples to fill prescriptions.

Among the abuses that have been found in the handling of physicians' samples are mix-ups of relabelled and mislabelled drugs; disregard of the expiration dates on antibiotics; and mixing together of physicians' samples from many sources without regard to codes, expiration dates, age of drugs, etc.

## Erythromycin side-effects

This antibiotic for oral use has been marketed by Lilly since 1958 under the name Ilosone. Recently cases of jaundice or abnormal liver function tests in people treated with this otherwise very effective drug were brought to the attention of the Government. The manufacturer right away revised its literature and sent a letter to physicians, headed "Drug Warning." It estimates that 15 million courses of therapy have been administered in the last three years and that 33 patients developed jaundice. Withdrawal of the drug has resulted in restoration of normal functions. In the letter to the physicians it was also said that no evidence exists as yet "that other available erythromycin salts are implicated in similar hepatic effects."

## Glucagon for insulin shock

This hormone is secreted by the pancreas; it increases blood sugar at the expense of liver glycogen by activating phosphorylase in the liver. In fact, it is an important regulator of blood sugar. Glucagon is now available for the treatment of insulin shock in diabetics and for terminating therapeutic insulin coma in psychotic patients. The *Medical Letter* (3 : 62) gives credit to the Eli Lilly company for its scientific contribution in purifying and studying glucagon.

The recommended dosage of glucagon for adults is 0.5-1 mg. administered parenterally.

## Foreign drug procurement restricted

Representative Richard Roudébush succeeded in modifying the U.S. government's \$4.2 billion foreign aid bill so that this money cannot be used for purchasing "patent-pirated drugs." This new law amounts to a victory of the young congressman over Senator Kefauver in his fight for changes in the American patent system. Rep. Roudébush plans to expand the legislation to prohibit use of any federal funds for purchases of drugs as well as any other kind of "pirated products"; for this purpose he introduced an "anti-pirating bill." He supported Pfizer's complaint about the "pirating of its tetracycline patents" in Italy, but has been fighting a losing battle against the U.S. armed forces which purchased this antibiotic from Pfizer's Italian competitors. According to the new law, purchases of drugs or pharmaceutical products manufactured abroad are barred, unless the manufacturer outside the U.S. is "expressly authorised by the owner of the patent."

Senator Kefauver promised to fight the new amendment in 1962—but for one year, at least, it will remain in force. The only permissible exception to the new law is a product which the Defence Department finds to be essential to the national security of the country.

## Plant and Equipment

### ►THERMOPLASTIC LABELLER

An 80 per min. fully automatic thermoplastic labelling machine has been designed and built by Newman Labelling Machines Ltd. It will apply labels to cylindrical or flat surfaces with very little changeover.

The containers pass through the machine in a straight line in continuous motion on a standard slat conveyor chain.

After passing through a gate mechanism the containers are engaged by a side pusher chain which controls them through the labelling station and discharges to a sponge faced presser belt. The activated labels are applied by a reciprocating hot plate which is moving in the same direction and at the same speed as the containers when the labels are applied.

For simplicity of changeover the label box and hot plate have constant top and leading edge label locations. Lateral positioning of the label on the container is accomplished by adjusting the pusher chain and vertical positioning by elevating the labelling head.

The machine is adjusted for container diameter or thickness by turning a single handwheel which opens the whole length of conveyor fencing.

### ►AUTOMATIC POWDER FILLING MACHINE

Arenco-Alite, who have used the container drop-away method of filling for many years in their tube filling machines, have now incor-

porated the same principle in an entirely new form of automatic powder filling machine.

The rigid container is taken to the filling station by means of a conveyor and, when under the filling tube, is raised so that the base of the tube is at the base of the container. At the same time a sealing former comes into contact with the top of the container. As soon as the fill begins to take place the container gradually drops away, thus keeping the base of the filling tube at the top level of the powder during the whole of the filling cycle. This method of filling has eliminated the problem of loose portions in the fill and air pockets, resulting in a compacted and accurate fill and a minimum of dusting. As the next container comes into position it is pushed under the filling tube, thus pushing the first and now filled container on to the take-away conveyor.

### ►50 GAL./HR. ION EXCHANGER

In 1935, two British chemists—Adams and Holmes—perfected the first practical ion exchange resins. When Rohm and Haas developed the mixed bed technique in 1952, ion exchange began to supersede the classical process of distillation for purified water. In 1955 Lorch introduced the cartridge type deioniser (Elgastat) and his method has become standard for provision of ultra-pure water in laboratory, research and teaching. The mixed bed cartridge deioniser does not require regeneration *in situ* and ensures

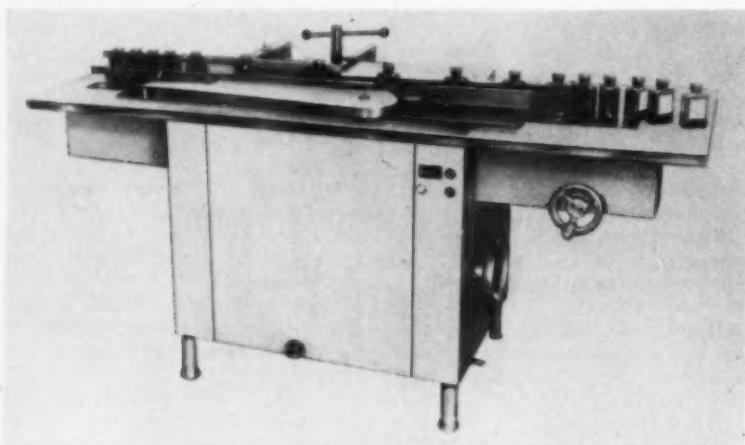


The standard model Fortune bottle and glass breaking machine fits on to an ordinary dustbin and consists of an aluminium funnel-shaped assembly, the base forming a dustbin lid. Mounted on this, a  $\frac{1}{2}$  h.p. electric motor drives the manganese steel bottle rotor which is housed in the lower portion of the funnel. Bottles broken and reduced at the rate of 600/hr. are then fed into the dustbin. Rubber buffers prevent any fly back. Standard model costs £46 15s., complete Cabinet model £63 15s. Supplied by Farrow and Jackson Ltd.

consistent effluent quality. In the same year Saunders presented "De-mineralised Water for Pharmaceutical Purposes" and in October 1955 the Pharmacopoeia Committee accepted deionised water in place of distillate, mainly on the basis of Saunders' recommendations. 1958 saw the adaptation of the Lorch process for the provision of intrinsic (approaching theoretical purity) water for transistor washing and Elgastats of this type are used in many semiconductor factories.

In chemical and pharmaceutical processes huge volumes of ultra-pure water are used throughout the working day, and for this purpose large ion exchange plants with efficient and often automatic regeneration fulfil the need.

Thus, two distinct and efficient techniques crystallised: the cart-



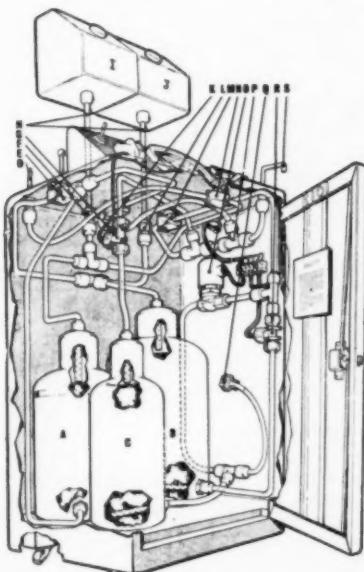
Automatic machine for thermoplastic labelling.

ridge type for small quantities of intrinsic water (10-200 gal./week) and the large mixed bed unit with regeneration *in situ* for bulk supplies (from 2,000 gal. up).

There is an obvious gap: a simple and foolproof deioniser for the chemist, pharmacist or research worker using 200-2,000 gal. of purified water per working week. To some extent this field was covered by conventional two-column and mixed bed demineralisers, but their working efficiency is low compared with cartridge type or large automatic plant. The Elga design team have now bridged this gap. Type E.101 produces ultra-pure or purified water B.P. at the rate of 50 gal. per hr. and regeneration is superseded by a simple charging cycle. An integral pre-purifier removes the gross contamination from the tap water and final "polishing" of the effluent is carried out by a mixed bed cartridge.

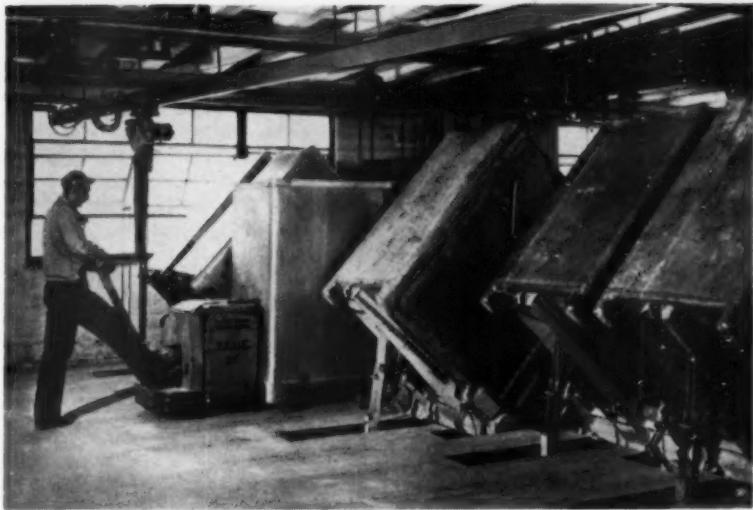
Elgastat Type E.101 embodies seven fundamentally new features:

1. It replaces manual regeneration by a semi-automatic charging cycle.



Type E101 Elgastat delivers 50 gal./hr. purified water B.P.

- A — Prepurifier columns.
- C — Elgelite C.209 mixed bed cartridge
- D — Mains water influent
- F — Cation charging fluid inlet
- G — Conductivity cell
- I — Cation charging fluid tank
- J — Anion charging fluid tank
- L — Anion charging fluid inlet
- N — Control valve
- Q — Mixed bed cartridge drain tube
- R — Prepurifier line cell
- S — Effluent point



Tote system of bulk handling enables operator to handle push-button station and quick interchange of bins. Empty bin is removed, full one put in its place ready for discharge, without interfering with discharge of other units.

2. Effluent quality is constant throughout the draw-off cycle (5 megohm-cm +).

3. Effluent cost is consistently low regardless of raw water quality.

4. This is the only mobile deioniser yielding 1,000 gal. between cartridge exchanges.

5. Unit size is that of a small filing cabinet, only a quarter of the measurements of an ordinary demineraliser with equal output.

6. Control valve, selector switch, recharging signal and a purity monitor have replaced the mass of ironmongery and columns commonly associated with demineralisation.

7. Type E.101 reaches the laboratory ready for use at a cost of £210 (no installation fee), some 65% saving compared with other deionisers of similar output.

#### ► BULK HANDLING SYSTEM

The Los Angeles Soap Co., which markets a range of soaps, detergents and water softeners in America, in 1958 installed a bulk-handling system for the ingredients of their *White King* water softener conditioner.

The method of handling used is known as the Tote system, which employs hermetically-sealed aluminium bins of 74 cu. ft. capacity, which may be used as shipping containers, storage units and discharge hoppers, with Tote tilts. These mechanisms tip the bins through an angle of 45°, enabling the contents to be com-

pletely discharged into either the process or packaging lines. Six such tilt stations have been installed for the handling of three basic ingredients of the water softener conditioner.

Switching from the method of handling materials in bags has resulted in savings, both in container and in labour costs.

The weight of the bin contents is determined by the nature of the ingredients which are non-hygroscopic and arrive in bulk hopper cars. They are screw conveyed to a drag-chain conveyor which carries them to the top of the building, where they are gravity discharged into Tote bins on various floors. At each of the filling stations an inverted Y arrangement is employed. As one Tote bin is filled, the filling spout automatically switches to the other. The full one is then placed in store. The new method saves time; the full unloading and storing of the contents of one bulk hopper car require a two-man-half-day.

The bins may be stored inside or outside, on any floor, and yet be readily available. Transport is effected by fork-lift truck, enabling 1½ tons of material to be automatically introduced into the production line in a few minutes. Subsequent operations are push-button controlled. Bins are discharged at several tilt stations.

The Tote system is available in the U.K. from Pressoturn Ltd., Leamington Spa, Warwickshire.

### Comprehensive Guide to Factory Law

By Robert McKoun. Chantry Publications, London. 1961. Pp. 124. 25s. net.

In this book the requirements laid down in nearly a dozen different Acts of Parliament and more than 200 Statutory Instruments, Certificates of Exemption, etc., have been arranged and indexed according to subject, so that the enquirer can see in a minute or two exactly what the law requires in any particular matter. Reference is also made to High Court decisions which have cleared up doubtful points, e.g. whether a canteen is subject to the Factories Acts and whether the requirements for the ventilation of workrooms apply to a boilerhouse.

The new edition has been revised to include the provisions of the 1959 Factories Act, the Clean Air Act, the Thermal Insulation Regulations, and other recent legislation, including the latest Food Hygiene Regulations. A supplement supplied in the form of a loose sheet inserted in the book anticipates the new Factories Act which will come into operation next April and which, without changing the law in any way, will alter the section numbers under which many of these requirements are made; this supplement shows the section numbers of the present Acts and the numbers of the sections covering the same requirements in the new Act.

### Practical Mycology

Manual for Identification of Fungi. By Sigurd Funder. 2nd Edn. Hafner Publishing Co., London. 1961. Pp. 144. 47s. 6d. net.

THIS is a second edition of the book reviewed in the March 1954 issue of MANUFACTURING CHEMIST, p. 122.

Changes are extremely slight, and therefore no further description is called for. But for those unable to refer to the earlier review it may be useful to know that the book gives an elementary but clear account of mycological technique and taxonomy, with clear line illustrations of the commoner fungal genera, including many of medical and agricultural interest.

The book is well produced, and will be appreciated by all beginners in mycology.

L. D. GALLOWAY.

### Extra Pharmacopœia—Supplement 1961

Pharmaceutical Press, London. Pp. 315. 32s. 6d. net.

This supplement brings up to date the 23rd edition of vol. 2 of Martindale published in 1955 and the 24th edition of vol. 1 published in 1958. The need for a supplement is amply justified by the ever-accelerating proliferation of medical and pharmaceutical knowledge.

The supplement covers analytical addenda, bacteriological and clinical notes, sterilisation, disinfectants, blood transfusion, proprietary medicine formulæ and new drugs and proprietaries. Particularly useful is the extra information on new drugs—over 200 of them—and new proprietaries—over 800—introduced since 1958. The formulæ of publicly-advertised medicines given in vol. 2 have been completely revised.

### Handbook of Chemistry and Physics

Ed. in Chief C. D. Hodgman. 42nd Edn. Chemical Rubber Publishing Co., Cleveland, Ohio. 1961. Pp. 3,481. \$12.50 net.

A book that has sold steadily over 46 years, most of that time as an annual publication, clearly has a faithful public. We all know that chemistry and physics are being more intimately related year by year. The chemist needs to know many of the data the engineer uses and vice versa. The book is in 11 parts: mathematical tables; properties and physical constants; general chemical tables; specific gravity and properties of matter; heat; hygrometric and barometric tables; sound, electricity and magnetism; light; quantities and units; and miscellaneous.

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The sections are divided by stiff green pages listing the contents. There is also an index.

This is a reference work of great merit which has the additional virtue of being brought up to date annually. One can sympathise with the publisher's problem of compressing a library of information into a single volume, but it is a pity that this necessitates the use of flimsy india paper. If the book were of larger format than the present 7½ in. x 6 in. and printed on better paper it would be much easier to use.

W.G.N.

### Biochemists' Handbook.

By Earl J. King and Warren M. Sperry. E. and F. N. Spon Ltd., London. 1961. Pp. 1,192. 168s. net.

This book presents in a concise form a wide range of biochemical data, arranged so that the reader can turn quickly to the information he needs.

The book has been compiled chiefly for the use of biochemists, both in the academic world and in industry, but it will also be found a useful work of reference by those engaged in closely allied fields: chemists, botanists, workers in the nutritional field, chemical pathologists and physiologists.

Since biochemists need to be familiar with certain aspects of chemistry and physiology as well as to be knowledgeable in their own subject, the relevant chemical data have been assembled at the beginning of this book and physiological data at the back, with the broad mass of biochemical data arranged between.

Thus, in Section I, the important topics in physical and organic chemistry which are most useful to biochemists have been included. Section II deals with enzyme kinetics and carries descriptions of about 300 individual enzymes. Section III is concerned with metabolic pathways. Section IV comprises data on chemical composition of animal tissues; and Section V contains comparable data for the plant kingdom. Section VI consists of information on some physiological and nutritional topics. The Handbook is completed by an index of over 60 pages.

### American Drug Index 1961

By C. O. Wilson and T. E. Jones. Pitman Medical Publishing Co. Ltd., London. 1961. Pp. 791. 55s. net.

THE American Drug Index has been prepared for the identification and correlation of the many pharmaceuticals available to the medical and allied professions. The need for this index has become acute as the number of drugs and drug products in all their tremendous variety has multiplied.

The organisation of the index is fundamentally alphabetical with extensive cross-indexing. Names listed are generic; brand (trade-mark, proprietary or speciality), chemical, U.S.A., N.F., N.N.D. and A.D.R. Synonyms that are in general use also are included. All names used for a pharmaceutical occur in alphabetical order with the pertinent data given under the brand name and the name by which it is made available. Data included are generic names, chemical names, manufacturer, pharmaceutical forms, size, dosage and use. Generic names occur in alphabetical order and here the recognition of the drug is indicated by U.S.P. (United States Pharmacopoeia), N.F. (National Formulary), N.N.D. (New and Non-official Drugs) and A.D.R. (Accepted Dental Remedies). The information is in accord with the latest of these books.

The cross-indexing feature permits the finding of drugs or drug combinations when only one major ingredient is known. For example, a combination of aluminium hydroxide gel and magnesium trisilicate is available. This combination can be found by looking under the name of either of the two ingredients, and in each case the speciality names are given.

### Nitric Acid

Manufacture and Uses. By F. D. Miles. Oxford University Press, London. 1961. Pp. 75. 9s. 6d. net.

THIS book has been prepared by I.C.I. with the assistance of the Science Masters' Association and the Association of Women Science Teachers, to teach students the difference between chemistry learnt at school and the chemistry used by industry.

Nitric acid is indispensable and it is odd that hitherto there has been no book in which the principles and practice of its manufacture have been discussed as a whole.

The author first outlines the evolution of modern methods of production, and briefly describes chemistry of the acid and of the nitrogen compounds related to it. He then deals with the physical chemistry of the reactions by which the acid is formed, and, from this, he points the way to an understanding of those elements of specialised engineering essential to the construction of manufacturing plants.

The construction and operation of two full-scale plants—one the most modern of its kind—are described in some detail and liberally illustrated by photographs and diagrams. In the last two chapters the methods of concentrating the acid are described and a concise account is given of its various applications.

### Industrial Chemistry

By W. Davey. Robert Hale Ltd., London. 1961. Pp. 110. 8s. 6d. net.

THIS book is intended to interest people in the chemical industry as a career. Accordingly the language is simple and the emphasis is upon the nature of different jobs in the chemical industry. In four chapters the author covers minerals and metals, natural products and fuels, and "synthetics," very briefly, of course.

The last two chapters discuss the work of the chemist and the chemical engineer and the employment of women in the chemical industry. Appendices list study courses available and addresses of universities and colleges. The book is quite cheap in order to be accessible to the young people who can best use it.

### Handbook of Organometallic Compounds

By Herbert C. Kaufman. D. Van Nostrand, Princeton, N.J. 1961. Pp. 1,550. \$22.50 net.

THIS work is of value not only to those already engaged in the field of organometallic chemistry, but also to those who are concerned with a multitude of commercial products which at present are not generally considered to be users of organometallics and organic compounds of such "non-metals" as S, P and N; e.g. biochemicals, cement, elastomers, explosives, fuels, lubricants, paints, pesticides, pharmaceuticals, photographic materials, and plastics.

The handbook lists in table form the physical and chemical properties of more than 12,000 organometallics, giving for each name, formulas, molecular weight, characteristics,

references and, wherever available, solubilities, vapour pressure, specific gravity, melting point, refractive index and/or molar refraction. The tables are arranged in chapters organised according to the periodic system. Each element's organic compounds can easily be found, since they are described under their empirical formulas.

Because comparisons of the physical-chemical constants of homologues are easily made with the help of these tables, it will be possible for research-minded users to predict the properties of as yet unknown organometallic compounds.

R.S.

### Warehouse Operations

By A. J. Briggs. John Wiley and Sons, London. 1961. Pp. 303. 68s. net.

THE movement and storage of goods accounts for anything up to 25% of their costs, so it is important that these essential facilities and services should be operated with the utmost economy and efficiency. This book aims to give the warehouse manager a guide to the planning, organisation and operation of his warehouse. There are plenty of photographs and drawings and the language is simple and direct. The pharmaceutical and chemical industries, which have their fair share of warehousing problems, should find the book valuable.

### Cell Function

By L. L. Langley. Reinhold, New York. Pp. 389, illustrated. \$7.50 net.

THIS introduction to the physiology of the cell and its rôle in the intact organism, by Professor Langley of the University of Alabama, is not concerned with cutting a broad path through all the biological principles so often found in textbooks of "general physiology"—the name chosen for many courses dealing with the principles governing living processes—but it concentrates on their fundamental units: the cells. Yet, in addition to the main chapters on the functional anatomy of the cell, the intracellular activities and the integration of the cells in the (mammalian) organism, there is also a section dealing with the basic background principles of cytology, such as physics, chemistry and mathematics—there are also many problems as well as literature references at the end of each of the 14 chapters of this interesting work.

RUDOLPH SEIDEN.

## Government orders foreign drugs

### Patents Act invoked to cut N.H.S. Bill

The Ministry of Health has placed contracts with four British companies for the supply of certain drugs in the broad spectrum antibiotic group which will come from manufacturers in Italy and Denmark. The contracts are for a period of one year and will operate from November 1, 1961. This recalls the Health Ministers' statement in May this year (MANUFACTURING CHEMIST, June 1961) whereby they announced his intention of invoking Section 46 of the Patents Act, 1949, in obtaining for the hospital service supplies of certain widely used drugs.

"Tenders for tetracycline, chlortetracycline, oxytetracycline, chloramphenicol and chlorothiazide have been considered and contracts for all of these have now been placed. It has been decided not to let a contract for the supply of hydrochlorothiazide for the present," reads the statement issued on October 2.

"All the successful tenderers are British companies but none is a patentee or licensee. The drugs to be supplied under the contracts will come from manufacturers in Italy and Denmark. They are of high quality, conforming in all respects to British standards. The claims of any patentees concerned will be considered and royalties negotiated as appropriate.

"It is not possible at this stage to give an estimate of the total savings which will result from this method of procurement."

#### A.B.P.I. statement

Following the announcement, the Association of the British Pharmaceutical Industry issued a statement which said the Minister's decision had been reached with the idea of buying drugs for hospitals at the cheapest possible price, regardless of the damaging effects on research and exports in the U.K. drug industry.

"There will be little or no encouragement for firms to maintain, let alone increase, research expenditure if hospital contracts for their most successful drug discoveries are to be awarded to unlicensed competitors.

"We are dismayed that the Health Ministers should thus seek to encourage foreign companies to manufacture abroad, for use in British hospitals, important drugs protected by British patents." The A.B.P.I. statement concluded with regret that the Ministers should have taken this step without prior negotiation.

The *Guardian* on October 3 stated that it was believed that the foreign

tenders were as much as £350,000 lower than the lowest from a British manufacturer, and mentioned that the representatives in Britain of the manufacturers who put in tenders on their behalf were Strang Chemical of Staines, Fraser Chemicals and Biorex Laboratories. It was expected that the Danish drugs would come from Marsing of Copenhagen, with which Strang Chemical is connected.

#### Pfizer's court action

As predicted last month (MANUFACTURING CHEMIST, October, p. 475) the Minister's action will be challenged in the High Court. The Pfizer Group has issued a writ to test the legality of the Minister's action. Pfizer say that the exercise of section 46 of the Patents Act constitutes a serious attack on the normal rights of the companies who own the patents concerned.

#### WHO urges control of drug advertising

People are easy marks for quackery and the blandishments of advertisers of medicines and drugs, for they know little about the structure and functioning of their bodies and yet are vitally interested in their own health and like taking things.

This is one of the main reasons that such advertising should be controlled, according to a survey of health legislation in pharmaceutical advertising published by the World Health Organisation,\* which reviews the situation in some 20 countries, most of them in Europe and the Americas.

The dangers of self-medication are made clear. There is always the risk of choosing the wrong drug, as, for example, an irritant purgative instead of an anti-spasmodic; of taking an excessive dose or too small a dose; of side-effects or of allergic reactions; of interfering with other drugs or of increasing their effect. There is also the possibility that the body will get used to a drug so that it loses its efficiency or becomes a habit, as well as the risk of suppressing the symptoms of an illness that could be cured if treated in time.

Another serious objection to pharmaceutical advertising is that it may create a pressing demand for a new remedy, sometimes even before doctors know about its existence, and before adequate tests have been made and the side-effects upon human beings are known.

The medical profession is aware of the dangers. The New York Academy

\* International Digest of Health Legislation, 1961, 12, 1-53.

of Medicine has voiced the opinion that the indications given in the advertising of tranquillisers were "frivolous," the hazards not stressed, and the claims for these remedies advertised in an extravagant and indiscriminate manner, without adequate warning about side-effects.

#### Employment for chemists: a 10 year prediction

By 1971 the chemical and allied industries may be employing 40,000 qualified chemists and chemical engineers, compared with 15,000 today. This guess was made by Sir Solly Zuckerman, scientific adviser to the Ministry of Defence and deputy chairman of the Advisory Council on Scientific Policy. He was speaking at the annual dinner of the Association of British Chemical Manufacturers in London last month.

His prediction was based on the use of professional manpower by the leading chemical firms today. If the prediction is correct, by 1971 8% of the payroll of the chemical industry will be qualified men, compared with 3.7% today and 2.7% in 1955. There appeared to be a good chance that these qualified men would be available because, said Sir Solly, we are now training more chemists and chemical engineers than the total of all science graduates before the war.

But even when the chemical industry does reach the 40,000 figure it will still be employing only the concentration of professional people working in the American chemical industry today.

#### Plant workers welcome Common Market

Speaking at the annual dinner of the British Chemical Plant Manufacturers' Association, held in London on October 25, the chairman, Mr. N. C. Fraser, stated that the Association supported the proposal that Britain should join the European Common Market. A European Trade Committee had been formed under the chairmanship of Mr. P. Seligman. During the last 12 months members of the Association had announced overseas contracts totalling over £12 million.

Sir Keith Joseph, M.P., Minister of State, Board of Trade, said: "In most lines if you can't sell your product abroad you soon will not be able to sell it at home either . . . because as tariffs come down—as they will whether we go into Europe or not—overseas producers will beat the non-competitive firm on its home ground." The proposal for profits tax relief for exporting firms had been considered by the government, but would undoubtedly break international agreements. Other countries, particularly Germany, which used to give an incentive of this kind, had abandoned it by agreement with the U.K.

# Meetings

## Institution of Plant Engineers

November 9. "Automatic Boiler Control for Medium and Small Size Boilers." 7 p.m. Roadway House, Oxford Street, Newcastle-upon-Tyne.

November 11. "Gas in Industry," by A. Mackenzie. 7.30 p.m. 25 Charlotte Square, Edinburgh.

November 14. "High-pressure Hot-water Systems," by A. E. Lock. 7.15 p.m. Manchester Literary and Philosophical Society's Rooms, George Street.

November 15. "Coal Utilisation," by Donald Hicks. 7 p.m. Sherwood Room, County Hotel, Theatre Square, Nottingham.

November 23. "Refractories for Boilers and Furnaces—Construction and Maintenance," by M. Ash and N. W. Hinchcliffe. 7.15 p.m. The Blossoms, Chester.

"Design and Installation of Gas and Chemical Plant." 7 p.m. Stockton-on-Tees.

## Society of Instrument Technology

November 13. "The Rôle of the Physicist in Plant Instrumentation," by L. J. R. Postle. 6.45 p.m. Literary and Philosophical Society, 36 George Street, Manchester 1.

November 16. "A Survey of the International Temperature Scale," by J. A. Hall. 6.45 p.m. College of Further Education, Greenhouse Lane, Loughborough.

November 28. "Automatic Plant Analysis by Electrochemical Methods," by R. F. Rodger. 6.30 p.m. Manson House, 26 Portland Place, London, W.1.

November 29. "Differential Producers for Flow Measurement," by H. E. Dall. Welsh College of Advanced Technology, Cathays Park, Cardiff.

December 4. "Problems of Flow Measurement," by H. E. Farrer. 7 p.m. Dept. of Fuel Technology, The University, Mappin Street, Sheffield.

December 8. "Instruments in Clinical Chemistry," by N. Crawford. "Electronics in Surgery," by R. Lightwood. 6.30 p.m. Lecture Theatre of the Byng Kendrick Suite, Gosta Green College of Technology, Aston Street, Birmingham.

December 13. "Instrumentation for Oil Fired Glass Furnaces," by N. I. Walker. 6.45 p.m. Literary and Philosophical Society, 36 George Street, Manchester 1.

## Royal Institution

November 10. "Modern Research on the Skin of Mice and Men," by W. S. Bullough.

## The Royal Society

November 16. Leeuwenhoek Lecture: "Interactions between Poxviruses," by F. J. Fenner.

## Royal Institute of Chemistry

November 29. A.G.M. 6.30 p.m. Shell Mex House, Strand, London, W.C.2.

November 30. "Chemical Aspects of the Work of the Warren Spring Laboratory," by C. C. Hall. 6.30 p.m. Battersea College of Technology, Battersea Park Road, London, S.W.11.

December 7. "Ultra-violet Spectroscopy," by T. M. Dunn. 6.30 p.m. Northampton College of Advanced Technology, St. John's Street, London, E.C.1.

## Society for Analytical Chemistry

November 15. "Chemical Services on British Railways," by G. H. Wyatt. 6.30 p.m. King's College, Newcastle.

"Recent Developments in Chromatography on Cellulose and Ion-exchange Cellulose," by N. F. Kember. 7.15 p.m. Royal Society of Edinburgh, George Street.

December 8. "The Structure of Natural Products by Direct X-ray Analysis," by J. Monteath Robertson. 7.15 p.m. Royal College of Science and Technology, George Street, Glasgow. "Analytical Research," by J. Haslam. University College, Cardiff.

## Chemical Society

November 9. "The Discovery of New Drugs," by A. F. Crowther. 8 p.m. Marischal College, Aberdeen.

"The Anatomy of the Chemist," by T. S. Stevens. 5 p.m. Edward Davies Chemical Laboratories, Aberystwyth.

November 10. "The Active Centres of Enzymes," by H. N. Rydon. 4.30 p.m. Chemistry Dept., The University, Birmingham.

November 13. "The Physical Chemistry of Ion-exchange Polymers," by E. Glueckauf. 5 p.m. University Chemical Laboratory, Cambridge.

"Surface Radiochemistry," by S. J. Thompson. 5 p.m. Science Laboratories, The University, Durham.

"Some Aspects of the Chemical Structure of Proteins," by H. D. Springall. 8.15 p.m. Inorganic Chemistry Lecture Theatre, Oxford.

November 16. "Some Studies in the Porphyrin Field," by G. W. Kenner. 5 p.m. Dept. of Chemistry, The University, Hull.

"The Biogenesis of Alkaloids," by Sir Robert Robinson. Conference Hall, Students Union, Chemical Society of Royal Technical College, Salford.

November 17. "Recent Developments in Acetylene-Allyne Chemistry," by E. R. H. Jones. 5.15 p.m. Washington Singer Laboratories, Exeter.

"Some Aspects of Cholesterol Biosynthesis," by G. J. Popjak. 4 p.m. Chemistry Dept., The University, Glasgow.

November 20. "Persulphate Oxidation

of Carboxylic Acids," by R. H. Thomson. 5 p.m. University Chemical Laboratory, Cambridge.

November 22. "The Stereochemistry of Flavan-4-ols," by E. M. Philbin. 5.30 p.m. Dept. of Chemistry, Trinity College, Dublin.

November 23. "Some Aspects of Structure and Reactivity in Ionic Solutions," by K. W. Sykes. 5 p.m. Dept. of Inorganic and Physical Chemistry, The University, Liverpool.

November 24. "Some New Photochemical Reactions," by D. H. R. Barton. 5.30 p.m. Dept. of Chemistry, Trinity College, Dublin.

"New Reactions in Dinitrogen Tetroxide," by C. C. Addison. 5.15 p.m. Chemistry Dept., The University, St. Andrews.

November 28. "Some Chemical Applications of Electron Resonance Spectroscopy," by H. C. Longuet-Higgins. 5 p.m. Dept. of Chemistry, The University, Nottingham.

November 30. "Aspects of the Biosynthesis of Phenolic Compounds," by C. H. Hassall. 6.30 p.m. Chemistry Lecture Theatre, The University, Leeds.

December 1. "New Reaction in Dinitrogen Tetroxide," by C. C. Addison. 4.30 p.m. Chemistry Dept., The University, Birmingham.

"Biphenylene and Related Compounds," by W. Baker. 8.30 p.m. University Chemical Laboratory, Cambridge. "The Gibberellins, a New Group of Plant Hormones," by P. W. Brian. 5.30 p.m. Chemistry Dept., King's College, Newcastle-upon-Tyne.

December 4. "Some Hydrogen Transfer Reactions," by H. B. Henbest. 5 p.m. University Chemical Laboratory, Cambridge.

December 7. "Microcalorimetry and the Thermogenesis of Living Species," by H. A. Skinner. 5 p.m. Edward Davies Chemical Laboratories, Aberystwyth.

"The Structure of Proteins," by M. F. Perutz. 6.30 p.m. Room F1, Manchester College of Science and Technology.

## Society of Chemical Industry

November 10. "Some Applications of the Adsorption of Gases by Solids," by K. S. W. Sing. 7.30 p.m. Lancaster and Morecambe College of Further Education, Torrisholme Road, Lancaster.

November 16. "The Chemistry of Glass and Glassmaking," by H. Cole. 7.30 p.m. Harris Institute, Preston.

"The Chemical Industry's Approach to Process and Plant Design," by J. M. Coulson. 6.30 p.m. Stephenson Building, King's College, Newcastle-upon-Tyne.

November 20. "Triazine Herbicides, their Chemistry, Biological Properties and Mode of Action," by H. Gysin.

#### MEETINGS (continued)

5.30 p.m. 14 Belgrave Square, London, S.W.1.

"The Structures which Limit the Penetrability of Skin," by R. T. Tregar. 6.45 p.m. Royal Society of Arts, 6 John Adam Street, London, W.C.2.

November 21. "Some Developments in Applied Oleochemistry," by M. Josephs. 6.30 p.m. O.C.C.A. Manchester Literary and Philosophical Society, 36 George Street, Manchester.

November 23. "Industrial Cell Culture and Vaccine Production," Barnes Hall, Royal Society of Medicine, Wimpole Street, London, W.1.

November 24. "Oxygen—Gaseous and Liquid—Its Production and Growth," by J. B. Smith. 7.30 p.m. Denbighshire Technical College, Wrexham.

"The Production of Organic Compounds labelled with C-14 or Tritium," by J. R. Catch. 6.30 p.m. 14 Belgrave Square, London, S.W.1.

November 28. "Hydrogen Bonding from a Crystallographer's Viewpoint," by J. C. Speakman. 4.30 p.m. Chemical Society, University Chemistry Dept., King's Buildings, West Mains Road, Edinburgh 9.

November 29. "Modern Electrochemistry and its Applications," by W. F. K. Wynne-Jones. 5.30 p.m. Chemistry Dept. University College, Upper Merrion Street, Dublin.

November 30. "Modern Electrochemistry and its Application," by W. F. K. Wynne-Jones. 7.45 p.m. Chemistry Lecture Theatre, Queen's University, Stranmillis Road, Belfast 7.

December 4. "Alkali Fusion of Fatty Acids," by B. C. L. Weedon. 7.15 p.m. Royal Station Hotel, Hull.

"Agricultural Fungicides," by D. Woodcock. 7 p.m. Houldsworth School of Applied Science, University of Leeds.

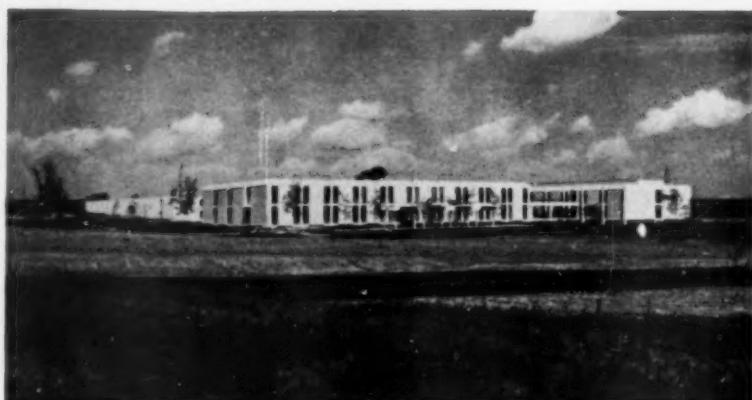
December 7. "Some Models of Physical Adsorption of Gases by Solids," by J. B. Smith. 7.30 p.m. College of Technology, Byrom Street, Liverpool.

"Adhesion and Adhesives," by A. Bramley and R. Pinfold. 7.30 p.m. Gas Showrooms, Parliament Street, Nottingham.

#### £100,000 grant for tropical anemias research

The Wellcome Trustees are to provide up to £100,000 to assist an integrated programme of research by several groups of workers into the severe anemias prevalent in tropical countries, with special reference to the malabsorption syndrome and tropical sprue.

The allocation comprises £45,000 to build and equip the Wellcome Laboratory of Tropical Haematology at Hammersmith; £14,000 to organise and maintain a scheme of close co-operation by visits and interchange of research material between the groups in Kenya, India, Hammersmith and



Three new buildings for McNeil Laboratories, part of the Johnson and Johnson group (U.K. affiliate McNeil Laboratories of High Wycombe), near Philadelphia, U.S.A., have a total floor space of 235,000 sq. ft. The buildings house administration, research and manufacturing departments and are constructed of reinforced concrete enclosed with off-white brick and precast concrete facing. Products of the company, soon to be marketed in the U.K., include Butisol sodium, a daytime sedative, Paraflex and Parafon, muscle relaxants, Flexin, for gout, Butibel, antispasmodic sedative, and Tylenol, paediatric antipyretic-analgesic.

Singapore led by Dr. Foy, Dr. Baker, Dr. D. L. Mollin of the Hammersmith Laboratory and an R.A.M.C. team in Singapore; £25,000 spread over five years for the continued support of Dr. Baker's unit in Vellore; and £15,000 for new X-ray equipment at Vellore.

#### Monsanto's European H.Q.

Monsanto Chemical Company of St. Louis, Missouri, U.S.A., has announced the establishment of a European H.Q. in Geneva by the company's wholly-owned subsidiary, Monsanto Overseas S.A. (MOSA). The move consolidates a number of company operations in Europe.

William M. Russell, president of MOSA, will be in charge of the Geneva operations. Also located at the Geneva headquarters will be William R. Haas, regional director of sales, now stationed in Paris, who will be responsible for MOSA's sales co-ordination throughout Europe; Dr. Charles H. Davenport, European technical representative at Geneva; and Donald B. Hirsch, manager of economic planning for Europe, who will join the organisation in Geneva at a future date.

#### Berk Pharmaceuticals merger

Berk Pharmaceuticals Ltd. has recently been incorporated by F. W. Berk and Co. Ltd. as a wholly-owned subsidiary to consolidate and develop their pharmaceutical interests. Trading of Leda Pharmaceuticals Ltd. has been taken over by Berk Pharmaceuticals and the staff absorbed by that company. Leda Pharmaceuticals Ltd. is another wholly-owned subsidiary of F. W. Berk and markets a range of pharmaceutical products.

Distribution of both Leda and Berk Pharmaceutical products will be handled from Berk House and bulk storage will continue at the Edmonton establishment. Research and development will be based on the Sandridge Laboratories.

A new pharmaceutical processing plant is scheduled for construction in the Home Counties.

#### Plasticiser project

Howards of Ilford Ltd., a member of the Laporte Industries Group, are undertaking two major projects.

The first is a new unit to make di-cyclohexyl phthalate, a solid plasticiser extensively used in the transparent packaging and film paper industries. Construction will start quite soon and completion is expected before the end of 1962.

The second project is the construction of a plant to produce cyclohexanol and cyclohexanone by the direct oxidation of cyclohexane with air. This plant will have an annual capacity of 9,000 tons of total products and the products will be sold by Howards as such or in the form of derivatives, e.g. dicyclohexyl phthalate, resins, cyclohexylamine, etc. It is expected that this unit will be completed by the end of 1963.

#### Change of address

The administrative and sales offices of the Yorkshire manufacturing companies in the Laporte Group are now accommodated at Eastgate House, Leeds 2. (Telephone: Leeds 32171. Telegrams: Laporte Leeds.)

Companies concerned are Laporte Acids Ltd., James Wilkinson and Son Ltd. and the Sheffield Chemical Co. Ltd.

## People

**Dr. J. L. S. Coulter** has been appointed medical director of Armour Pharmaceutical Co. He was formerly director of medical studies and medical officer-in-charge of the Royal Navy Medical School.

**G. F. Edwards** has been appointed general manager (production) by F. W. Berk and Co. Ltd. He will be responsible to **F. A. Rivett**, director, for all production at the company's works at Stratford, Baynards (Sussex), Wolverhampton, Swansea, Sandridge, London Colney and Edmonton. Mr. Edwards' headquarters will be at Abbey Mills, Stratford, E.15.

**D. S. Gardner** has been appointed to succeed the late **E. L. Pipe** as foundry sales representative in the Midlands, South Wales and the West.

William R. Warner and Co. Ltd. have announced the appointment of **A. G. Johnstone** to the Ethical Division as marketing executive. Prior to joining Warners, Mr. Johnstone was with the Pharmaceutical Division of I.C.I.

**J. A. W. Gill** has been appointed a director of Steele and Cowlishaw Ltd., Hanley, Stoke-on-Trent. Mr. Gill will retain his position as manager of the chemical machinery sales department of Baker Perkins Ltd., of Peterborough, the parent company of Steele and Cowlishaw Ltd.

**Samuel W. McCune III**, deputy managing director of the Du Pont Company (United Kingdom) Ltd., has been promoted to managing director.

Mr. McCune succeeds **William H. McCoy**, who returns to the U.S.A. on special assignment with the parent company in Wilmington, Delaware.

A graduate in chemical engineering of Princeton University, Mr. McCune joined the parent company in 1940 as a chemist in the company's rubber laboratory and was transferred to the Du Pont Co. (U.K.) Ltd. as general sales manager in 1957.

Durazone-Choice have announced the appointment of **W. Loring** as aerosol development chemist. Mr. Loring will be working on the further development of the Durazone-Choice range aerosols and on the introduction of a number of new products. He will also be responsible for the formation of a research laboratory equipped to deal with the aerosol problems of outside companies.

**L. H. Welch**, who retired recently from the position of chief electrical engineer to the London Electricity Board, has been appointed as industrial



Dr. J. Ferguson



W. Loring

relations consultant to the Electrical Research Association.

Mr. Welch has been closely connected with the work of the E.R.A. for many years, especially with that on cables and insulating oils. In his new appointment Mr. Welch will be acting as advocate for co-operative research in the electrical industry.

**Dr. John Ferguson**, research and development Director, is retiring from the main board of I.C.I. Ltd. on November 30, after 33 years' service with the company.

Dr. Ferguson went from Stirling High School to Glasgow University, and undertook research at Bristol and Oxford Universities before joining I.C.I. in 1928.

Dr. Ferguson was a director and research manager of Alkali and General Chemicals Divisions and later became joint managing director, a post he held until 1957, when he joined the main board of I.C.I. as research director. For a time he was also group director for the Alkali and General Chemicals Divisions. In 1961 he assumed directorial responsibility for development as well as research.

**Dr. W. O. Alexander**, assistant research manager, of I.C.I. Ltd., Metals Division, has been appointed technical director of Foseco International Ltd. with effect from January 1, 1962.

Foseco International Ltd. is a subsidiary of Minerals Separation Ltd.

The Plessey Co. Ltd. have appointed **A. A. Evans** sales manager of the Capacitors and Resistors Division, Swindon. Previously, Mr. Evans was Swindon regional sales administrator. He joined the company in 1958.

The U.K.A.E.A. have announced the appointment of **H. V. Disney**, at present deputy managing director, as managing director of their Engineering Group to succeed **J. B. W. Cunningham**, who is resigning from January 20, 1962.

James A. Jobling and Co. Ltd., Sunderland, have appointed three new executive directors: **I. T. F. Cochrane** (marketing), **S. Waring** (distribution) and **N. W. Vickers** (engineering).

The company manufactures *Pyrex* glassware for scientific/industrial use.

**Geoffrey Phillips** has been appointed public relations officer of British Hydrocarbon Chemicals Ltd. The post at B.H.C. is a new one: the company, jointly owned by British Petroleum and the Distillers Co., is a rapidly expanding organisation in the petrochemicals field.

Mr. Phillips is well known in industry for his work as National Secretary of the British Association of Industrial Editors.

The Wellcome Trust have announced the retirement of **Lancelot Claude Bullock**, who was appointed a trustee under the will of the late Sir Henry S. Wellcome, who died in 1936. For many years he was senior partner in the city firm of solicitors, Markby, Stewart and Wadeson. He is succeeded by **Robert Malleson Nesbitt** of Markby, Stewart and Wadeson.

The Home Office have appointed **J. Stephens** Secretary of the Poisons Board in place of **C. G. Jeffery**.

Nicholas Laboratories Ltd. have appointed **Gordon R. Fryers** managing director, **Victor M. Bond** finance controller and secretary, and **Carl Norman** controller of international operations.

Shell Chemical Co. Ltd. have announced the retirement recently of **E. E. Bullen**, finance director. He is succeeded by **W. F. Tuson**, who will be known as director, finance and economics, and the company's economics and planning department, under **A. J. Gait**, will report to him.

### Leonard Hill manager wins publishing prize

**David Kingham** of Leonard Hill Ltd. is one of the two winners of an award from the Young Publishers Association. The award is a trip to the United States to printers, publishers, binders, wholesalers and packers to gain an insight into the American publishing and printing trade.

The two Young Publishers leave on November 25 for their three-week visit. Mr. Kingham is manager of circulations and book sales at Leonard Hill Ltd. and has been book department manager for three years. He was one of the two members of the Association who made the best impression on a judging panel, with a written review of their publishing career and an interview.

### Government report on chemical industry plans

The board of Trade has completed a report on long-term planning in the chemical industry. It was prepared with the help of certain leading members of the industry. The report is apparently one of several prepared to help implement the Government's proposals to bring Britain's economic growth in line with that of other countries. The slowness of our expansion is a major political argument between the Government and the Opposition.

The existence of the chemical industry report was mentioned by the chairman of the A.B.C.M., Sir William Garrett, at the association's meeting last month. But no further details were given to MANUFACTURING CHEMIST upon enquiry at the A.B.C.M. and the Board of Trade. It is not certain that the report will be published.

### New A.B.C.M. chairman

Successor to Sir William Garrett is Mr. J. C. Hanbury, of Allen and Hanburys Ltd. The Vice-Chairman is Mr. M. J. C. Hutton-Wilson (Associated Chemical Companies Ltd.) and the Honorary Treasurer is Mr. J. L. Harvey, M.B.E., D.L. (The Fullers' Earth Union Ltd.).

### DSIR Research Council

The Minister for Science, Lord Hailsham, has appointed five new members of the Council for Scientific and Industrial Research. They are L. H. Bedford, G. B. R. Feilden, F.R.S., Professor E. R. H. Jones, F.R.S., Professor O. A. Saunders, F.R.S., and H. C. Tett. Three members who have completed their five-year term of office retired recently: the former chairman, Sir Harry Jephcott, Professor C. E. H. Bawn, F.R.S., and Sir Willis Jackson, F.R.S. Sir Walter Drummond has been reappointed for a period of three months.

Other members of the Council are: Professor B. Bleaney, Professor C. F. Carter, Dr. J. W. Cook, Frank Cousins, Vice-Admiral Sir Frank Mason, Dr. C. J. Smithells, and Lewis T. Wright. Chairman: Sir Harold Roxbee Cox. Secretary: Sir Harry Melville.

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\* THE DECEMBER ISSUE \*  
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\* Here are some of the articles \*  
\* you can read in next month's \*  
\* " Manufacturing Chemist " \*  
\*  
\* THE NEW PENICILLINS \*  
\* STOP VALVES FOR CHEMICAL DUTIES \*  
\* FINE CHEMICALS FROM COAL TAR \*  
\* SMALL-SCALE MIXERS \*  
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### New oral penicillin

A new penicillin, active like Celbenin against "resistant" staphylococci, but suitable to be taken by mouth, has been synthesised at the Beecham Research Laboratories. Called by its code number BRL 1400, the new penicillin is one of a group of related penicillins synthesised from 6-amino penicillanic acid, the penicillin nucleus first isolated and made just under three years ago at the Beecham Research Laboratories.

Reports on BRL 1400 were given recently to a medical symposium in New York, organised by Bristol Laboratories, who have been licensed to produce the drug under a Beecham patent.

### Bulk storage and delivery service

F. W. Berk and Co. Ltd. have appointed E. G. Jewell to be responsible for advising and assisting customers who wish to use the company's bulk delivery service.

Bulk storage of liquids in tanks not only ensures continuity of supply but also eliminates the cost of handling returnable containers. In many cases tanks can be constructed in less space than is required by stacked containers, and, particularly where underground tanks are permissible, valuable space can be made available for other purposes.

### THE CHEMICAL MARKET

#### This month's changes

There are few changes in price this month. Citric acid is down £20 per ton. Mercurial chemicals also showed a downward trend. Among the metals, tin rose by £10 a ton, copper remained firm at £228 10s., and quicksilver dropped £2 per flask.

Chinese menthol continued to drop by 2s. 6d. to 60s. lb. Little change was shown in essential oils, apart from citronella which rose slightly to 6s. lb.

### European chemical market research association

Representatives of chemical companies from seven countries at a meeting in Paris last month (October) decided upon the formation of a chemical market research association for Europe. Companies represented included F. W. Berk, Montecatini, I.C.I., Hoechst, Du Pont, Esso Petroleum, Shell International Chemical, Mobil Oil and Union Carbide.

A second meeting will be held in London early next year, which will be open to all interested in European chemical market research who may wish to attend.

### THE TECHNICAL PRESS IN NOVEMBER

## Instrumentation and Control

**Food Manufacture** publishes a review of instruments and control equipment for food processing in addition to an article, "Food Canning in Argentina." There is a report on "Food Manufacture in Norway."

**Chemical and Process Engineering** features high-pressure processes with two articles: "Calcium reactor vessels" and "Fabrication of stainless steel pressure vessels in Sweden." Mixing is the subject of a unit operations review. Another article in the series on constructional materials for chemical plant features rubber.

**World Crops** deals with driers and process machinery. Articles include "Grain Drying," "The Phytotron," "From Bullock to Tractor" and "The Pruning of Coffee."

In **Paint Manufacture** this month there is an article, "Recent Advances in Phthalocyanine Pigments," and a description of Colloidal Silica as a thickening agent for paints. Other articles discuss "Colorimetric Assay of Lead," and the "Application of China Clay in the Paint Industry."

**Dairy Engineering** deals with advances in tanker design for bulk pick-up and there is a review of bulk collection equipment. Articles include "Swiss Success with Aseptic Filling of Uperised Milk" and "Tank Cleaning on the Farm and in the Dairy."

**Petroleum** prints a special review of U.K. refineries this month. Other articles are: "Safe Handling of Flammable Liquids," "Digital Computers Lower Refinery Maintenance Costs" and "World's Largest Crude Pipe Still Controlled by Computer."

**Muck Shifter and Bulk Handler** reports on machinery stocked and hired by local authorities. Other titles are: "Tunnel or Bridge—the alternatives for the Channel crossing and the advantages and disadvantages of each," and "Tractors work in Gypsum Mines."

**Conferences and Exhibitions** describes selling to America and French specialised exhibitions.

**Corrosion Technology** discusses wire rope corrosion and corrosion in transmission and distribution.

**Automation Progress** contains an article on The Cryotron—a superconducting computer component, and an item on Maintenance for Automation.

For specimen copies apply to the Circulation Manager, Leonard Hill House, Eden Street, London, N.W.1.

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P6916

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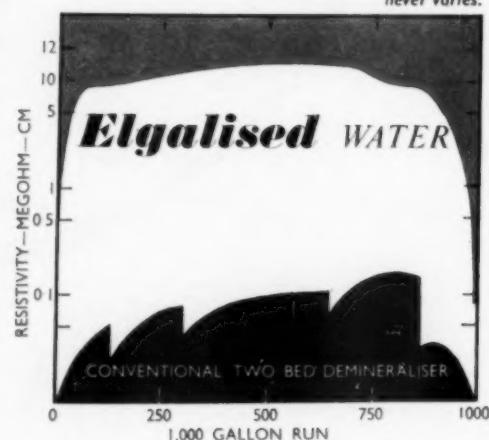
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[K]

## News from Abroad

### U.S.A.

#### Anglo-American plastics agreement

*Tusplus*, the chemically bonded laminate of unplasticised P.V.C. and polyester resin reinforced with glass fibre, developed by Tough Plastics Ltd. in the U.K. and Europe, is now to be made in the U.S.A. Haveg Industries Inc., of Wilmington, fabricators of chemical plant in various plastic materials, have signed an agreement with Tough Plastics Ltd. and will manufacture and sell *Tusplus* in the U.S.A.

### GHANA

#### Hungarian aid for pharmaceutical plant

On the basis of an agreement between Hungary and Ghana for the delivery of several plants, the first pharmaceutical factory is to be shipped to Ghana by the Hungarian foreign trading company Komplex. The factory will be built in Accra according to Hungarian plans and will serve in the future as the basis for the development of an independent pharmaceutical industry. The factory will be equipped to manufacture tablets, dragees and injections. It will employ about 200 persons.

Construction work will be directed by the Chinein pharmaceutical factory of Hungary. Primary materials and equipment, including a phial-marking machine, which is semi-automatic and capable, with a capacity of 3,500 pieces per hr., of marking phials in two colours, will be supplied by Hungary.

The plant is due to start production in 1963.

### BURMA

#### Snake menace

Snakes in Burma fleeing the rising waters caused by recent heavy rains have created a serious menace. Cobras, kraits and vipers are the main danger. The Burmese Government has urgently requested the World Health Organization to help in the purchase of 2,000 ampoules of anti-venom serum for treating casualties.

### ARGENTINA

#### Pharmaceutical imports increase

In the first seven months of 1961, Argentina's imports of pharmaceutical products totalled US\$96,400,000, as compared to US\$38½ million in the corresponding period of last year, an increase of 99%.

### AUSTRALIA

#### Control of narcotics

A more effective control of imports into Australia of narcotic drugs is covered by amendments to the

Customs Regulations. Minister for Customs and Excise, Senator Henty, said they included additions to the list of prohibited drugs or narcotics which Australia was obliged to control under international commitments.

To avoid misunderstandings, the list has been rearranged into alphabetical order, and each drug has been described by its internationally recognised, non-proprietary name.

#### Drug industry facts

Latest official statistics show that at June 30 there were 503 factories in Australia producing chemicals, drugs, medicines and toilet preparations. Employees numbered 22,214, and the year's salary and wage bill totalled £24,220,000. Land and buildings were valued at £11,528,000, while plant and machinery was worth £5,347,000. During the year additions to land and buildings cost £3,413,000, while additions and replacements to plant and machinery cost £8,981,000 (depreciation of the latter was listed at £4,588,000). Average annual salary and wage per employee was £1,096; average value of production per person engaged was £6,648; and ratio of salaries and wages to value of production was 33.42 per cent. Value of raw materials used was £69,523,000; cost of power, fuel, light, etc., was £5,684,000; and total value of output was £147,689,000.

#### Merck project

A pharmaceutical factory is to be built in the Sydney suburb of Granville by Merck Sharp and Dohme Inc. at a cost of £445,000. This new factory will replace the present pharmaceutical plant at Fairfield.

#### Curb on chemists

The New South Wales Government has decided to replace its Pharmacy Act with legislation similar to that of other States, which will prevent anyone except a qualified pharmacist owning and operating a chemist's shop. The provision is designed to prevent the development of pharmacy chains owned by unqualified people who engage pharmacists as managers. However, unqualified persons who owned such shops before the introduction of this new legislation will be exempt, but when they die their shops will have to be sold within twelve months. No pharmacist or partnership of pharmacists will be able to own or control more than one pharmacy.

#### Titanium oxide contract

Laporte Titanium Ltd. has awarded to the Bechtel Organisation (Bechtel Pacific Corporation Ltd., Melbourne; Bechtel International Ltd., London) the

overall contract for engineering and construction of the titanium oxide plant to be built for them at Bunbury in Western Australia.

The plant is designed to produce annually 10,000 tons of titanium oxide pigment, the major portion of which will be shipped to the Eastern States of Australia to supply the growing demand for titanium oxide by the paint, paper, plastics and associated industries.

### SPAIN

#### $H_2O_2$ plant

Laporte Chemicals Ltd., a subsidiary of Laporte Industries Ltd., has entered into an agreement with the Spanish Company, Peroxidos S.A., to provide technical assistance and advice on the construction of an autoxidation hydrogen peroxide plant near Saragossa in Spain.

The initial capacity of the plant will be 1,000 tons of hydrogen peroxide annually (calculated as 100%). Production is planned to start in 1963, subsequently rising to 1,500 tons.

Peroxidos S.A. have been incorporated in Spain to deal in chemicals and chemical products and, in particular, all grades of hydrogen peroxide.

### SOUTH AFRICA

#### Castor oil seed development

A £50,000 plan to develop castor oil seed cultivation is being launched in the Orange Free State goldfields area. The oil will be used in the manufacture of pharmaceuticals, greases and paints.

#### Beecham's new factory

Steady progress is being made on the erection of the new factory for Beecham South Africa (Pty.) Ltd. at Johannesburg. The building, with plant and equipment, will cost £300,000. It is planned to close the Cape Town factory at the end of this year and concentrate all manufacturing at Johannesburg.

### LIBYA

#### Soap factory

A contract has been signed between the Libyan Industries Co. and a German soap manufacturing firm to set up a factory to cost more than £100,000.

### INDIA

#### Smallpox protection

Twenty thousand vaccinators are being recruited by the Government of India for a mass vaccination campaign against smallpox. The campaign will start shortly and is to protect India's 430 million inhabitants. WHO is assisting the country in the manufacture of freeze-dried vaccine. This campaign is part of the world smallpox eradication programme launched by WHO.



## Shell Process Oils are backed by Shell Service

Shell have a comprehensive range of mineral hydro-carbon process oils with a diversity of physical and chemical properties to suit all needs. These oils are obtained from a variety of crudes which are processed by various refining methods, and include technical white oils and liquid paraffins and petroleum jellies of B.P. quality, ideal for use in cosmetic, toilet and pharmaceutical preparations.

Shell Ondina and Risella Oils are highly refined technical white oils of good colour stability, and Shell Diloma Compounds D and K are first quality white and yellow petroleum jellies. These products

are highly saturated, stable materials, suitable for the manufacture of toilet and cosmetic preparations.

Shell Light Liquid Paraffin B.P., Shell Liquid Paraffin B.P., Shell White Petroleum Jelly B.P. and Shell Amber Petroleum Jelly B.P. all meet the requirements of the British Pharmacopoeia and are supplied for medicinal and pharmaceutical purposes.

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Shell Process Oils Section  
Shell-Mex House, Strand  
London, WC2



# SHELL PROCESS OILS

# Packaging

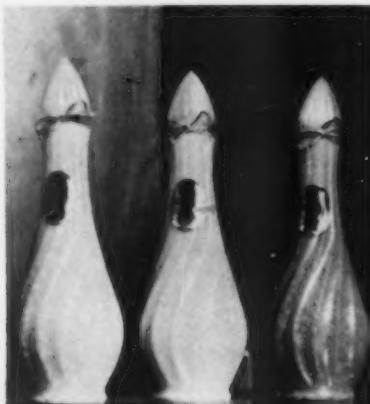
## Cutter and creaser

The débüt of the first two-revolution cutter and creaser with a standard in-built stripping unit was made at the showrooms of Gordon and Gotch Ltd. recently.

The machine, the Viking 48 cutter and creaser, which has just been added to the range of Tifring and Viking presses by the Swedish manufacturers, Grafiska Maskin Aktiebolaget, has a maximum sheet size of 37 by 50½ in., a speed range of 1,000 to 3,300 i.p.h., and it will handle a variety of stock from paper to 0.040 in. board. The manufacturers claim that it has distinct advantages over platen machines, particularly when cutting larger sizes, paper, thinner boards and wavy stock.

The weight of the machine is considerably less than a comparable platen cutter and creaser. The principle of cylinder cutting allows for a clean incision and excellent register without the violent platen action and the resultant forces and stresses, and the strength to weight ratio is considerably higher.

The frame parts are extremely heavily dimensioned. There are separate supporting beams themselves directly supported on the main centre beam. The forme bed, which is made of cast iron, has intersecting reinforcement ribs which provide an extremely low-weight construction with a considerably increased resistance moment. The weight of the moving parts is so low that it enables considerably higher cutting speeds to be attained. The air buffers are provided with a compensation cylinder which makes a more favourable cycle of operation possible at retardation and acceleration of the cutting forme.



Bath crystals made by Perfumerie Delafine Ltd. are packaged in diagonally fluted Poly-Tainer polythene bottles which will not break, by Metal Box. The bath crystals are available in three perfumes, lavender, rose and verbena, price 4s. 6d.



**Christmas soap packs.** Left: batch tablet of Cullingford soap moulded and hand painted as Popeye with white cord attached for use in bath and shower. Right: Cussons six-colour litho printed pack for Imperial Leather soap.



**"Two Step"**

**New shampoo from Gibbs is packed in unique divided bottles and in double sachets with twist-off necks. First lathering is done with deep cleaning blue shampoo, the second with "lanolin-gold to ensure silkiness and manageability." Bottle costs 3s. 3d.; sachet 11d.**

The drive of the reinforced cylinder has a world-patented split gear that eliminates the back lash in the lower and upper position of the cylinder, an important factor in registration.

The cut and creased blanks are delivered from the cutting cylinder on to the stripper feed table, where they are re-registered automatically and fed between a pair of stripping rolls. These are driven by the main press and work on a two-revolution cycle. As each blank passes through the rolls the waste portions of the sheet are pierced by pins and carried downwards, being subsequently ejected by the peeling sheet. The remaining portion is fed on to the delivery tapes to be stacked and piled in the normal way. The stack is of very high accuracy as all outside trim is removed by the stripper.

The stripping method is simple, and a make-ready machine is included in the equipment to enable the user to make up stripping patterns while the press is running.

The Viking 48 cutter and creaser with the stripping unit is 33 ft. long (21 ft. 11½ in. without the stripper), 9 ft. 1½ in. wide and 7 ft. 1 in. high. It weighs 24,250 lb.

## Cartoning machines

Flexible Metal Co. Ltd., Stevenage, are agents for Costruzioni Automatiche Martelli (CAM) of Bologna, Italy, for their range of packaging machines. The range of CAM cartoning machines includes Models *Pr* and *Pri*, which will handle cartons of the following dimensions: Width, ½ to 3½ in. Depth, ½ to 1½ in. Length, 2 to 5½ in. These models will carton all tubes, small bottles, soaps, phials, suppositories, etc. Model *P2r* will handle cartons 1½ to 4 in. wide, ½ to 2½ in. deep and 3½ to 7½ in. long. Special attachments include a device for inserting a leaflet with the product, for wrapping the product with protective corrugated cardboard, and for applying a thermoplastic pilfer-proof seal. The *Pr* and *Pri* models are claimed to carton 4,000 to 7,000 cartons per hour; the *P2r* will handle 3,600 to 6,000 per hour.

Other CAM machines include a wrapping and sealing machine for airtight packaging of small products and a filling and cartoning machine for powder or granular products.

## Strip-packagers

German Wolkogon strip-packaging machines exhibited recently by Gordon and Gotch include the TVC/U, which counts and packs 12,000-14,000 tablets per hr. and the MS/II, which heat-seals printed covers around 8,000-12,000 cellophane and aluminium strips per hr.

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## New Products

### Two pharmaceuticals from Berk

Two new pharmaceutical products have been introduced by Berk Pharmaceuticals Ltd. *Asilone*, a tablet containing 0.250 gm. of a polymethylsiloxane for the treatment of intestinal distension, heartburn and medicamental gastritis, is supplied in polystyrene boxes of 12 tablets, price 5s., plus 11d. P.T.

*Acdrile*, an enteric coated tablet of cysteine methyl ester hydrochloride for the treatment of chronic bronchitis and other respiratory tract conditions, is supplied in bottles of 28 tablets, each 0.1 gm., at 15s., plus 2s. 9d. P.T.

Both products are obtainable on prescription only.

### Seven-in-one vaccine for sheep

The Wellcome Foundation's *Covexin* system of protection for sheep against soil-borne diseases enables the sheep farmer to provide immunisation against seven diseases in one vaccine. The product, resulting from ten years' research, protects sheep against lamb dysentery, pulpy kidney disease, strick, braxy, blackleg (post-parturient and wound gangrene), black disease and tetanus.

Previously, the sheep farmer has needed to use a number of single vaccines to protect his flock against the main clostridial diseases. With *Covexin*, the number of injections necessary in the first three years of the animal's life will be reduced from 12 to five or six.

The new vaccine is claimed to cut feeding time for lambs by a month, since formerly lambs had to be weaned on to better pastures gradually, because sudden access to lush food precipitated disease. *Covexin* will also enable the farmer to time all inoculations to coincide with normal shearing, marking gatherings, and thus reduce labour costs.

A bottle of *Covexin*, costing 75s., provides 50 injections, each of 5 c.c.

### Improved Procion dye

I.C.I. Dyestuffs Division have introduced Procion Brilliant Red H3BNS, which is homogeneous and represents, for textile printing purposes, a major improvement on the earlier Procion Brilliant Red H3BS. It is said to have better solubility (100 p.p. 1,000 of print paste as compared with 40 p.p. 1,000) and better build-up and washing-off properties.

The product should find application on silk and on chlorinated wool, in addition to use for printing cellulosic fibres.

### Sulphur dispersant for viscose spinning

*Lubrol CB* is a new viscose spinning bath additive developed and marketed by the Dyestuffs Division of I.C.I. It is

claimed to possess negligible affinity for cellulose and affinity losses from the spinning bath are therefore virtually eliminated. At the same time, the product, in spite of its relatively weak cationic character (it is a substituted polyamine/ethylene oxide condensate), has excellent sulphur-dispersing power and good stability under spin bath conditions.

*Lubrol CB* is liquid and readily forms clear solutions in water, spin bath liquor, 6% caustic soda or in viscose dope. It is non-ionic in alkaline media and weakly cationic in acid media, and is therefore compatible with anionic, non-ionic and cationic agents under alkaline conditions and with non-ionic and cationic agents under acid conditions.

The amount of *Lubrol CB* to be added depends on the type of produce being made, varying from 0.2-0.8 kg. per ton of product (0.02-0.08%) in the case of viscose rayon staple fibre to 1.5-3 kg. per ton (0.15-0.3%) in the case of tyre cords. Intermediate quantities are suitable for cast sheet (viscose transparent film) or for continuous filament viscose rayon. It exercises a beneficial lubricating action which reduces and stabilises yarn tension and so minimises breakages and inhibits corrosion of lead parts of the equipment. In the tyre cord process *Lubrol CB* can usefully be employed as a viscose coagulation retardant.

### Influenza vaccine

Glaxo Laboratories Ltd. state that their 1961-62 influenza vaccine, *Invirin*, supplies of which are now available, is designed to give protection against the type of influenza most likely to be encountered during the coming winter.

The Asian strain and the "B" strain components are the same as previously, but in addition there is a third strain, A/England/1/61, isolated last winter during the heavy, local influenza outbreaks which developed principally in the Midlands and the North.

Vaccination is by a single injection (half dose for children) and maximum protection takes about two weeks to develop. It is claimed that an effective degree of immunity will persist for up to about six months. The vaccine costs 10s. per 1 ml. ampoule.

The British Safety Council is again recommending its 7,000 member industries (employing some four million workers) to carry out mass-vaccination to prevent large-scale absenteeism.

### Oral analgesic

Burroughs Wellcome and Co. have issued a new potent oral analgesic, *Diconal* tablets, available in 25's and 100's at 6s. and 17s. 6d. respectively, subject to the usual discount.

*Diconal* Tablets supersede *Pipadone* compound tablets, which will no longer be issued.

### Perfumed deodorant

A perfumed stick and spray have been added to the *Go* range of deodorants, to partner the perfumed roll-on deodorant introduced last year by Potter and Moore Ltd.

Lightly scented so as not to clash with other perfumes or colognes worn, the stick and spray cost 3s. and 3s. 6d. respectively. Refill sachet for the spray costs 2s. 6d.

Both packs have the distinctive colour scheme of pink, white and black, and the *Go* spray is in a new plastic squeeze bottle with a screw-on top that ensures against leaking.

### Stored grain insecticide

Cyanamid of Great Britain Ltd. have developed two new Malathion insecticide formulations for use in grain storage: Cyanamid Malathion Wettable Powder (a 25% formulation), and Cyanamid Malathion Grain Protectant (a 2% Malathion dust).

Since Cyanamid first discovered malathion in 1949 this organo-phosphorus insecticide has been widely used all over the world.

### Skin ointment

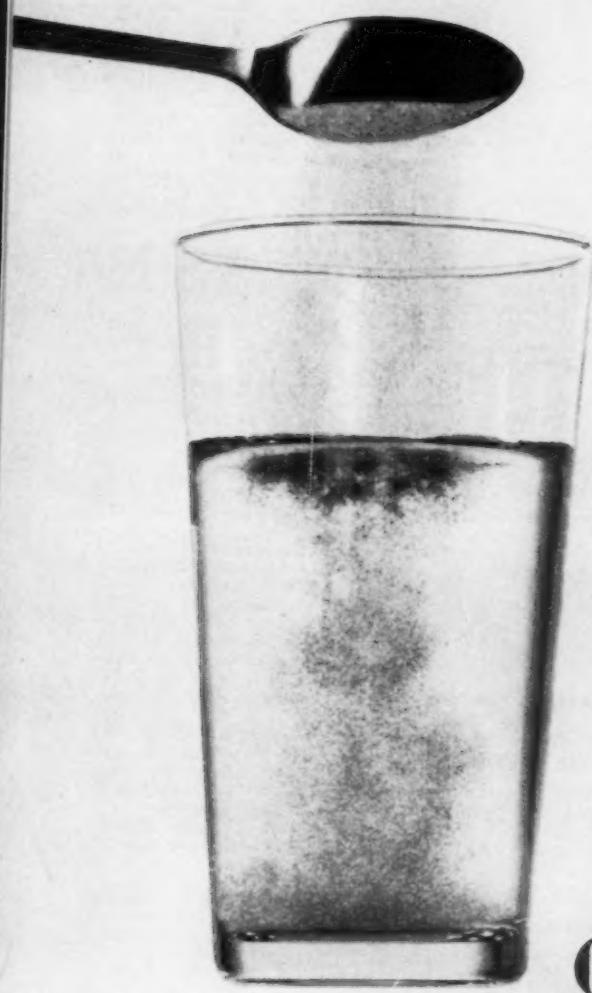
Merck Sharp and Dohme Ltd. have extended their range of *Hydrocortone* ointment to include *Hydrocortisone* (*Hydrocortone*) ointment  $\frac{1}{2}\%$  B.N.F. (greasy base). The price structure is the same as for the existing *Hydrocortone* non-greasy cream and similarly will be available in 5 g., 15 g. and 50 g. packs.

The full range now available is *Hydrocortone* non-greasy cream and greasy ointment in  $\frac{1}{2}\%$ , 1% and  $2\frac{1}{2}\%$  strengths in 5 g. and 15 g. tubes and 50 g. jars. The product will have a new clip-on type of detachable label to facilitate dispensing.

### Cerebral sclerosis treatment

A new product for the treatment of cerebral sclerosis, *Cosaldon*, has been introduced by West Pharmaceutical Co. Ltd. *Cosaldon* tablets contain a new xanthine derivative SK7 (1-hexyl 3 : 7 dimethylxanthine) which is claimed to be different from other xanthines in that it is fat soluble, has a mild sedative action and cerebral vasodilation properties. Nicotinic acid has been included in the formulation because it has been shown to potentiate the action of SK7.

The basic N.H.S. cost of one week's maintenance dosage is 1s. 11d. and the tablets are available in bottles of 100.



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minute  
flat!**

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Remarkable new Kraystay gels; stabilizes; suspends; thickens; emulsifies. The secret is the strikingly efficient and edible emulsifying agent, carrageen moss. Special techniques have been developed in America for harvesting this rare and valuable product in bulk. Kraystay's uses in manufacturing industries are almost limitless. It is compatible with most compounds; goes completely into solution at 165°F; and its special properties help you produce a smoother more consistent product, with great economy. And Kraystay has many extra advantages over and above its unique emulsifying properties. For instance, when used in creams it automatically forms a microscopic film to prevent the unused cream from drying out, and also greatly improves 'handslip'. Kraystay is available in 10-lb, 20-lb and 200-lb drums—at competitive prices.



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Or write for details.

HCI

## NEW TRADE MARKS

### APPLICATIONS

#### Cosmetics and toilet preparations

CORIALON.—808,589. *Hans Schwarzkopf*.  
 ESTARINUM.—813,270. *Edelfettwerke Werner Schlüter*.  
 BLOSSOM.—813,950. *Thomas Hedley and Co. Ltd.*  
 PETAL.—816,047. *Thomas Hedley and Co. Ltd.*  
 PRESENCE.—816,068. *Société de Distribution de Parfumerie et Cosmétique "Diparco" S.A.*  
 LIQUISUN.—805,307. *Ellanby Laboratories Ltd.*  
 COOL.—806,126. *Miners Make Up Ltd.*  
 FRESHMEN.—816,011. *Myram Picker Ltd.*  
 GYRO.—816,968. *Thomas Hedley and Co. Ltd.*  
 BLUE PETER.—817,346. *Ingasseter Ltd.*  
 EIPON.—817,915. *Brentford Soap Co. Ltd.*  
 TAFFETA MIST.—818,954. *Charles Bedeman Ltd.*  
 LAURAMINE.—809,470. *Dutton and Reisch Ltd.*  
 TRIFT.—811,236. *Hans Ströbeck Aktiebolag*.  
 FERIL.—815,589. *Lever Brothers, Port Sunlight, Ltd.*  
 GAYAL.—815,592. *Hudson and Knight Ltd.*  
 MAYBORN.—815,794. *Mayborn Products Ltd.*  
 LADY X.—816,782. *Thomas Hedley and Co. Ltd.*  
 GOLD STAR.—817,015. *Brentford Soap Co. Ltd.*  
 MARAUDER.—817,393. *Balfour Laboratories Ltd.*  
 NIADENT.—817,449. *County Laboratories Ltd.*

#### Pharmaceuticals

PENTRACYN.—804,647. *Société d'Etudes, de Recherches et d'Applications Scientifiques et Médicales S.A.*  
 PINEXO.—806,931. *Dumas Milner International Inc.*  
 EDI-SPEL.—807,554. *The British Products Sanmex Co. Ltd.*  
 LATEXADOR.—808,775. *Industrial Pictures Ltd.*  
 GESTORAL.—809,326. *Organon Laboratories Ltd.*

### Manufacturing Chemist's ENQUIRY BUREAU

Leonard Hill House, Eden Street, London, N.W.1.

Subscribers requiring names of suppliers of chemicals or plant should state their needs on this form, giving approximate quantities, clip it to their business noteheading and send it to the Bureau, as above. Please type or use block letters.

For office use

No.

Date

## NEW PATENTS

### COMPLETE SPECIFICATIONS ACCEPTED

#### Miscellaneous

Tertiary amines. *Farbenfabriken Bayer A.G.* 876,465.  
 Preparation of urea-dialdehyde starch derivatives. *Miles Laboratories Inc.* 875,542.  
 Alkali metal salts and alkaline earth metal salts of N<sup>1</sup>-isonicotinylhydrazine N-glucuronide and a process for the production. *Chugai Seiyaku Kabushika Kaisha*. 876,607.  
 Modified furfural-aldehyde resins. *Farbwurke Hoechst A.G.* 876,087.  
 Allo-ocimeno and its derivatives. *International Flavors and Fragrances Inc.* 875,685.  
 Process for the production of 2-halogenocycloheptene-(1) carbocyclic acids-(1). *Badische Anilin- and Soda-Fabrik A.G.* 876,121.  
 Pyrimidine derivatives. *Imperial Chemical Industries Ltd.* 876,601.  
 Production of hydrogen peroxide. *Food Machinery and Chemical Corporation*. 876,459.  
 Organic salts of substituted quinolines and process for the manufacture thereof. *Chemische Fabrik Schweizerhall*. 876,678.

Process for the production of hydrazine hydrate. *Farbenfabriken Bayer A.G.* 876,038.  
 Production of unsaturated aliphatic nitriles. *Distillers Co. Ltd.* 876,446.  
 Process for the preparation of branched-chain aliphatic carboxylic acids or their derivatives. *Henkel and Cie G.m.b.H.* 876,450.  
 Production of alkyl pyridines. *R. S. Aries*. 876,747.  
 Pyrimidines. *Imperial Chemical Industries Ltd.* 875,717.  
 Calcination of alumina. *Dorr-Oliver Inc.* 876,597.  
 Cyclopentanophenanthrene derivatives and process for the production thereof. *Syntex S.A.* 876,903.  
 Preparation of acetonedicarboxylic acid and esters thereof. *Chas. Pfizer and Co. Inc.* 876,487.  
 Process for the manufacture of uridine and thymidine derivatives and compounds concerned therein. *F. Hoffman-La Roche and Co. A.G.* 875,971.

New patents are from the *Journal of Patents*, and new trade marks are from the *Trade Marks Journal*. In each case permission to publish has been given by the controller of Her Majesty's Stationery Office. Each of the publications mentioned is obtainable from the Patent Office, 26 Southampton Buildings, London, W.C.2.

## NEW COMPANIES

These particulars of new companies have been extracted from the daily register of Jordan and Sons Ltd., company registration agents, Chancery Lane, London, W.C.2.

**Edward Magraw Ltd.** 15.8.61. 15/17 Wigan Road, New Springs, Wigan. Chemists etc. £4,000. Dirs.: Edward and Mrs. A. Magraw, 15 Sittingbourne Road, Wigan.

**Fernstraw Products Ltd.** 15.8.61. 34 Nicholas Lane, E.C.4. Mnfrs. of and dlr.s. in chemicals, dyestuffs, etc. £500. Dirs.: Sydney H. Newman, James A. Burgess and Ernest O. Hampton.

**Les Parfums Godet (Great Britain) Ltd.** 15.8.61. 82z Portland Place, W.1. £100. Subs.: Myrna F. Hillel and Linda Cohen.

**John E. Jagger (Hassocks) Ltd.** 16.8.61. 10 Brunswick Road, Shoreham-by-Sea, Sussex. Chemists, etc. £100. Dirs.: Ida K. Green and Norman H. Collyer.

**Uncle Ben's Ltd.** 16.8.61. 48 London Fruit Exchange, E.1. Chemists, etc. £100. Dirs.: Montague Haberfield and Monty I. Cohen.

**Van Vleck and Olivers Ltd.** 21.8.61. 94 Rickmansworth Road, Watford. Chemists, etc. £100. Dirs.: Charles W. Tragan and Ada F. Earl.

**Franklin Developments Ltd.** 11.9.61. Research, development and experimental chemists, etc. £1,000. Dirs.: Not named. Subs.: Cranston G. Walton and Peter E. Greed.

**Forestral Industries Ltd.** 12.9.61. Chemical and plastics mnfrs., mfg. chemists, etc. £100. Subs.: J. B. A. Willis and D. W. Dare (solrs.), 18 Austin Friars, London, E.C.2.

**Bligh and Dobson Ltd.** 13.9.61. 188 Old Lane, Leeds 11. To take over the bus. of retail chemists cd. on at Leeds as "Bligh and Dobson," etc. £100. Dirs.: Michael I. Bligh and Eric Dobson.

**E. Silverberg and Co. Ltd.** 13.9.61. 231 Breck Road, Everton, Liverpool 5. Chemists. £100. Dirs.: Eric A. and Fanny Silverberg.

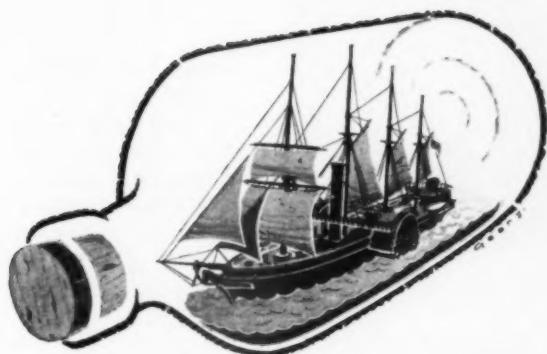
**H. M. Gardner Ltd.** 13.9.61. Pharmaceutical chemist cd. on by the execs. of Henry M. Gardner deceased at Bridge St., Stafford, etc. £12,000. Dirs.: Marjorie V. and Ann M. Gardner, 37 The Oval, Stafford.

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 November 1896

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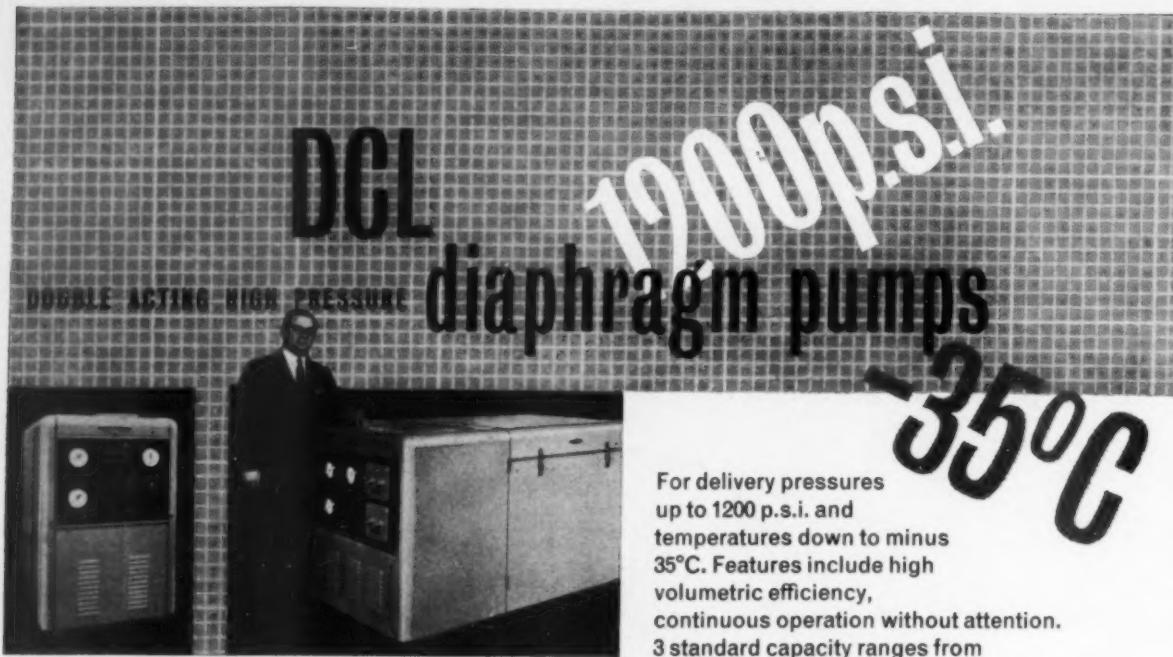
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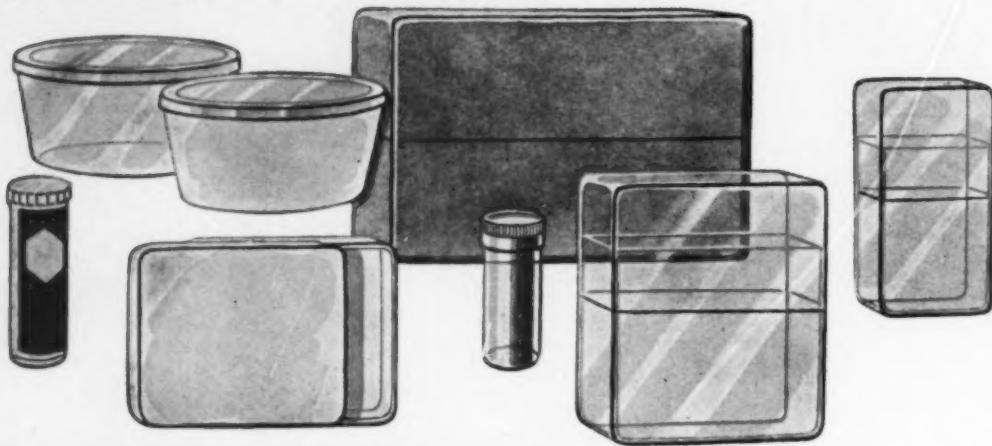
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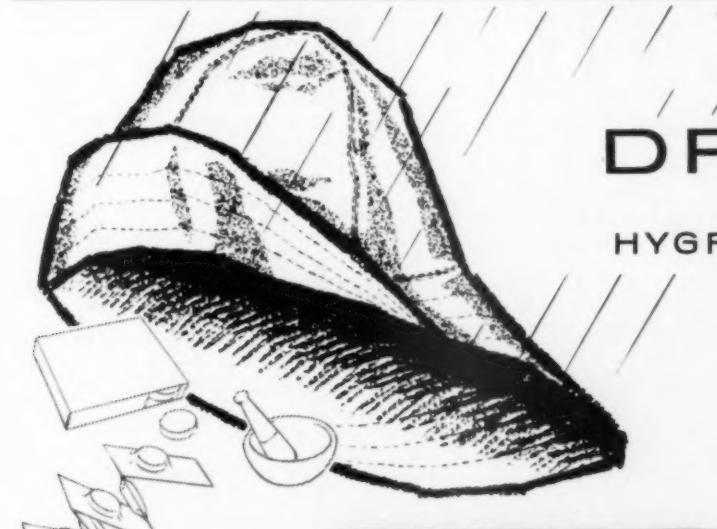


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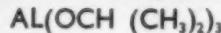
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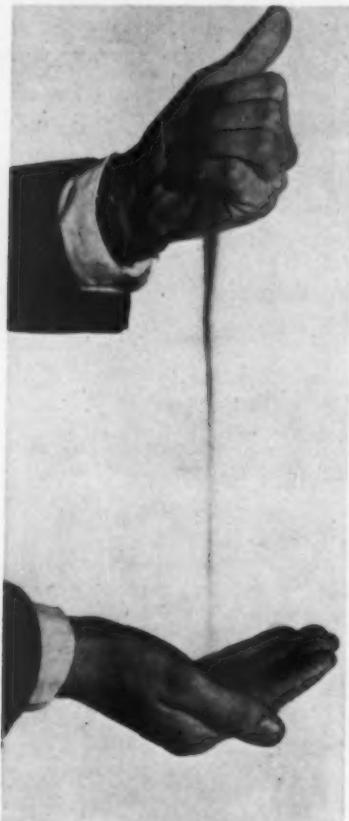
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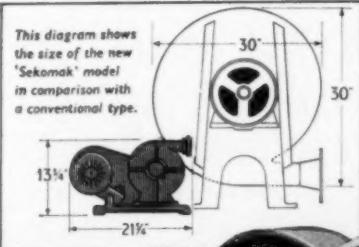
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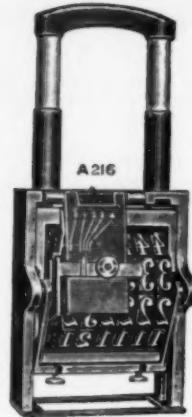
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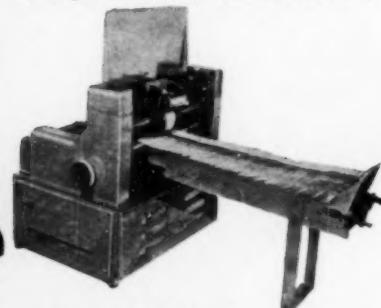
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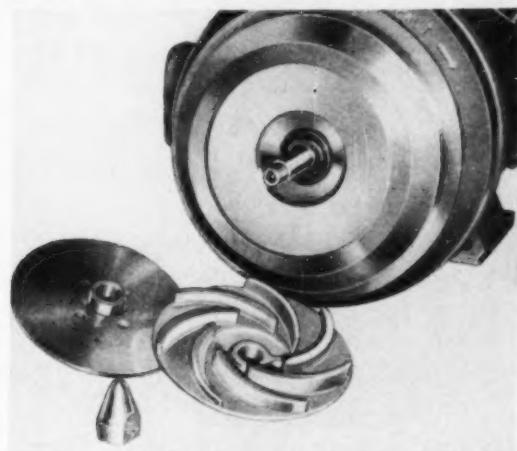
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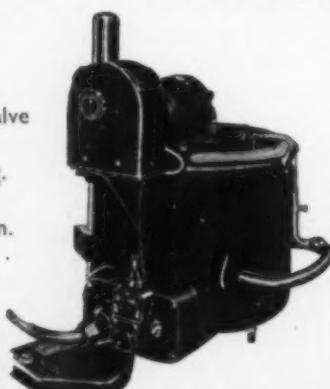
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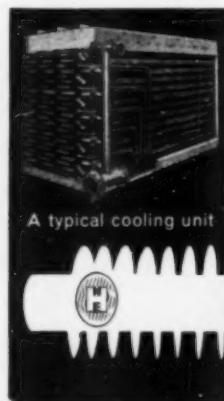
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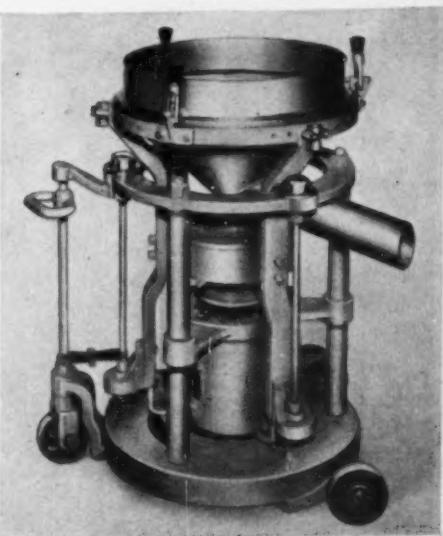
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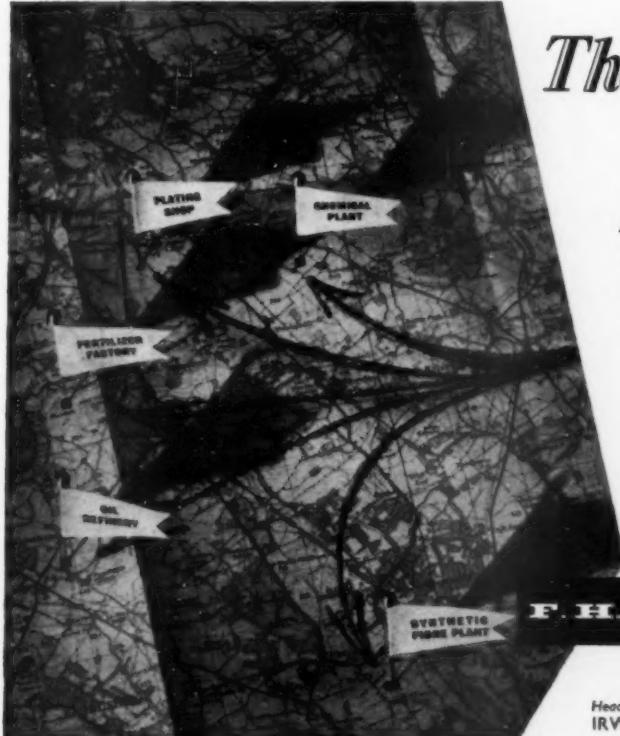
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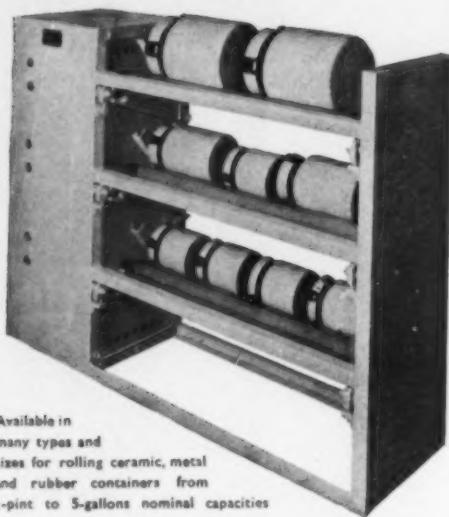
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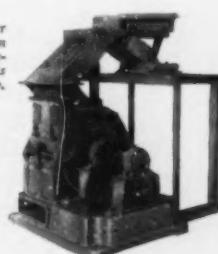
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(continued on page 107)

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(continued next col.)

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*Post (a):* duties—inspection of surgical instruments and operating theatre equipment at manufacturers' works, and assisting in development of new types of instruments and equipment; qualifications—Licentiate of the Institute of British Surgical Technicians, or 10 years experience in design or manufacture of relevant equipment or instruments, or experience as instrument curator in a hospital.

*Post (b):* duties as above in respect of dental equipment and instruments; apprenticeship (or equivalent training), or 10 years experience, in design or manufacture of dental instruments or equipment essential.

*(c)—2 posts* mainly for routine inspection of pharmaceutical products, chemicals, blood transfusion apparatus, and surgical and ward dispensary sundries; also technical record-keeping and assisting in preparation of specifications. Qualifications: at least O.N.C., or equivalent, in Chemistry or Applied Chemistry; ability to use laboratory equipment and make simple chemical tests and measurements; knowledge of rubber technology an advantage. Inner London salary scale £1,064-£1,246. Promotion prospects. Write Civil Service Commission, 17 North Audley Street, London, W.1. for application form quoting S/5399/61. Closing date 15th December 1961.

# I.S.I.S. Appointments Register

Licensed annually by the L.C.C.

9, Eden Street, London, N.W.1. EUSton 5911.

I.S.I.S. is an organisation backed by a large industrial group of consultants with contacts in all the industries based on technology. As an addition to their present resources they have established this Appointments Register. Below will be found some of those technologists who are looking for further opportunities. Employers and Personnel Officers are invited to complete the form below, detach and send to the above address. In this particular instance the use of a form, with its attendant simplification of office systems, ensures speedier results for the employer.

Ref. B.382. Irish. Male. Married. Age 26. RESIDENT ENGLAND. B. Eng. 5½ yrs. Ass't Engr., consulting Engrs. At present Ass't Engr., consulting (civil) engrs. Consid. exper. design & detail work on R.C. & genl. harbour & steam power station design & on site supervising construction bldgs., roads, railways & services. Seeks post as SITE ENGR., with civil engg. contractors. London. £1,200 p.a.

Ref. B.383. British. Male. Married. Age 38. Assoc. Inst. Science Technology. M.R.S. Health. 1 yr. Student Technician & 2 yrs. Junr. Technician, tropical medical research. 6 yrs. Senr. Technician & 5 yrs. Chief Technician, virological research. 10 yrs. Research Superintendent/Supt. Medical Research Technologist, tropical virus research. At present Superintendent, Medical Research Technologist (Virology), tropical medical research. Consid. exper. design & devpt. research labs., prod. of medical films, qualified installation of medical refrigeration—high vacuum systems. Seeks post as CHIEF EXPERIMENTAL OFFICER/MEDICAL REPRESENTATIVE. S.W. England, London or abroad. £1,600 p.a. min.

Ref. B.386. British. Male. Married. Age 30. Resident Africa. B.Sc. (Agric.) Hons. 1½ yrs. Agric. Officer & District Plant Protection Officer, Indian Govt. At present Agric. Officer i/c Expt. Sugarcane Estate, Africa—experimental experience on sugarcane, weedkillers, fertilisers, insects, pests & disease control. Seeks post as RESEARCH WORKER. U.K. or any Commonwealth country. £1,200/£1,500 p.a.

Ref. B.388. British. Male. Married. Age 38. A.M.A.S.E.E. Studying C. & G. Telecommunications. 4 yrs. Apprentice, elec. engrs. 11 yrs. Elec. Inspector (Supervisory), aircraft mnfrs. At present Test Engr.—design & devpt.—elec. switchgear & appliances. Seeks STAFF POST. U.K.—not London. £1,000 p.a.

Ref. B.390. British. Male. Married. Age 39. Exper. includes 7 yrs. Inspector, telecommunications. 10 yrs. self-employed, radio. 3 yrs. Inspector, acoustic engg. 20 yrs. Head of Eng. Laboratory, telecommunications. At present Head of Engg. Lab., London (chem. engg.), telecommunications. Seeks post in TELECOMMUNICATIONS ENGG. London (S. or S.E. pref.). £1,000 p.a.

Ref. B.395. British. Male. Married. Age 28. C. & G. (Radio Comms.). 3 yrs. Electronic D/man. 2 yrs. Ass't Section Leader & 3½ yrs. Section Leader, electronics. At present Senr. Design D/man, electronic equip't. Seeks post as SENR. ELECTRO/MECH. D/MAN. London. £20 per week.

Ref. B.396. British. Male. Married. Age 26. B.Sc. (Zoology). At present Editor of scientific journal. Seeks post pref. as PLANT NEMATOLOGIST, but would consider post dealing with pest control or parasitology. Anywhere considered. £900 p.a.

Ref. B.400. British. Male. Married. Age 44. Inter. B.Sc. 3 yrs. Lab. Ass't & 2 yrs. Chemist, cellulose & synthetic dept., paint mnfrs. 2 yrs. Chemist, plastics mnfrs. 3 yrs. Foundry Analysis Chemist, motor vehicle mnfrs. 3 yrs. Chemist, printing ink mnfrs. 1 yr Chemist/Works Manager, lacquer mnfrs. At present Chemist/Ass't. Works Manager/Celulose Dept. Manager, french polish, cellulose lacquer & varnish mnfrs. Author of published Technical articles. Seeks post as CHEMIST/WORKS OR PROD. MANAGER. S. London area. £1,200/£1,500 p.a.

Ref. B.402. British. Male. Married. Age 42. Nat. Inst. Eng. Dip. 16 yrs. Air Engr., R.A.F. 4 yrs. Workshop Instructor, steam turbine mnfr. At present Examiner i/c Aeronautical Inspection, aeronautical engg. Seeks SUPERVISORY (ENGG.) POST N. England. £18 per week.

Ref. B.403. British. Male. Married. Age 42. Dip. in Agric. M.I.C.A.M. Exper. includes 6 yrs. Tenant Farmer. 4 yrs. Area Manager, seedsman. & 3 yrs. Fertiliser Adviser, fertiliser mnfr. At present Fertiliser Advisor, fertiliser mnfr. Freelance agric feature writer & broadcaster. Wide exper. organising agric. demonstrations & meetings. Seeks post as ADVISORY SERVICES MANAGER (SEEDS, FERTILISERS). U.K.—pref. S. England, but would consider abroad. U.K. salary £1,500 p.a.

Ref. B.404. British. Male. Married. Age 27. H.N.C. (Mech. Eng.). 6 yrs. Apprentice/Junr. D/man, special purpose m/cs, packaging. 6 months. D/man, electro-mech. devices. 3 yrs. Design D/man, plant devpt. At present Design D/man, electrode mnfrs., arc welding, m/cs & accessories. Seeks post as JUNR. ENGR./SALES ENGR. City or N. London. £1,000 p.a.

Ref. B.406. British. Male. Married. Age 41. B.Sc. (Mining). 1st Class Colliery Manager's Cert., N.A.C.M. 6 yrs. Colliery Manager & 3 yrs. Colliery Agent. At present Mines Superintendent—coal, iron, manganese limestone, abroad. Exper. controlling isolated stations & of water supply, hospitals, housing. Seeks post as ENGG. ADMINISTRATOR/MINE SUPT. U.K. or abroad—not Africa.

Ref. B.408. British. Male. Single. Age 29. O.N.C. (Mech.), 5 yrs. Apprentice, aircraft mnfr. At present

Project Designer, aircraft mnfr. Seeks post as DESIGN D/MAN. London or abroad. £1,050/£1,100 p.a.

Ref. B.74. British. Male. Married. Age 37. G.C.E. 'A' level Chem. & Physics H.N.C. (Chem.). 3½ yrs. Laboratory Technician, medical laboratory. 5 yrs. Senr. Research/Devt. Chemist & 10 yrs. Laboratory & plant Manager, fine chemicals. At present Senr. Research Devt. Chemist, chem. mnfrs. Consid. exper. mnfr. & process devpt. of inorganic salts of almost all elements in the periodic table. Seeks post as LABORATORY OR PLANT MANAGER (pref. Research & Devpt.). U.K.—Provinces or S. England. £1,500 p.a.

Ref. B.409. British. Male. Married. Age 30. Apprenticeship & 3½ yrs. practical toolroom exper. At present Prod. & Tool Devpt. Engr., motor vehicle mnfrs. Exper. of marine engg. Seeks post as TECHNICAL REPRESENTATIVE. U.K. £1,000 p.a.

Ref. B.411. British. Male. Married. Age 40. 2 yrs. Trainee, inter. communications. 4 yrs. Expert Manager, silk mnfrs. At present Installation Planning Engr. electronics—radar, radio, TV, transmitters, land/marine communications equip't. Exper. customer liaison, collation of information. Seeks TECHNICAL SALES/CUSTOMER LIASION/SALES ADMIN. OR PROMOTION POST. Europe. London, S. England, or S. America. £1,300 p.a.

Ref. B.412. British. Male. Married. Age 27. Studying for O.N.C. 5 yrs. Apprentice, motor engns. 1½ yrs. Bench Fitter, motor mnfrs. At present Junr. Design D/man, automotive & special purpose m/c work, design & devpt. engrs. Seeks post as TECHNICAL REPRESENTATIVE, based on Luton area.

Ref. B.472. British. Male. Married. Age 29. 3rd. yr. C. & G. Standard. 1 yr. Tracing & Dwg. Exper. 13 yrs. Electrician, electrical contractors. At present Electrician, elec. instn. Seeks post as ELEC. D/MAN. Essex or S.E. London. £750 p.a.

Ref. B.474. British. Male. Married. Age 26. O.N.C. Mech. Engr. with Prod. endorsements, 1st yr. H.N.C., C. & G. M/c Shop Engg. Genl. Works Apprenticeship, followed by training & work in Plastics R. & D., & metal finishing research with special ref. to plating & effluent plant layout & design. At present Pilot Plant Supervisor, light engg. Seeks TECH. SERVICES/LIAISON/TECH. REP. POST. Herts. Middx. pref., but will consider elsewhere. £1,000 p.a. min.

To: I.S.I.S. Appointments Register, 9, Eden Street, London, N.W.1. Please ask the following applicants to communicate with the undersigned:

Ref.:

Please use Block capitals

Name:

Position:

Company:

Business or Profession:

Address:

All introductions are made on the understanding that should an engagement result the employer agrees to I.S.I.S. Appointments Register's terms, which are as follows:

For each person engaged the equivalent of two weeks salary payable by the employer within fourteen days of the date of engagement.

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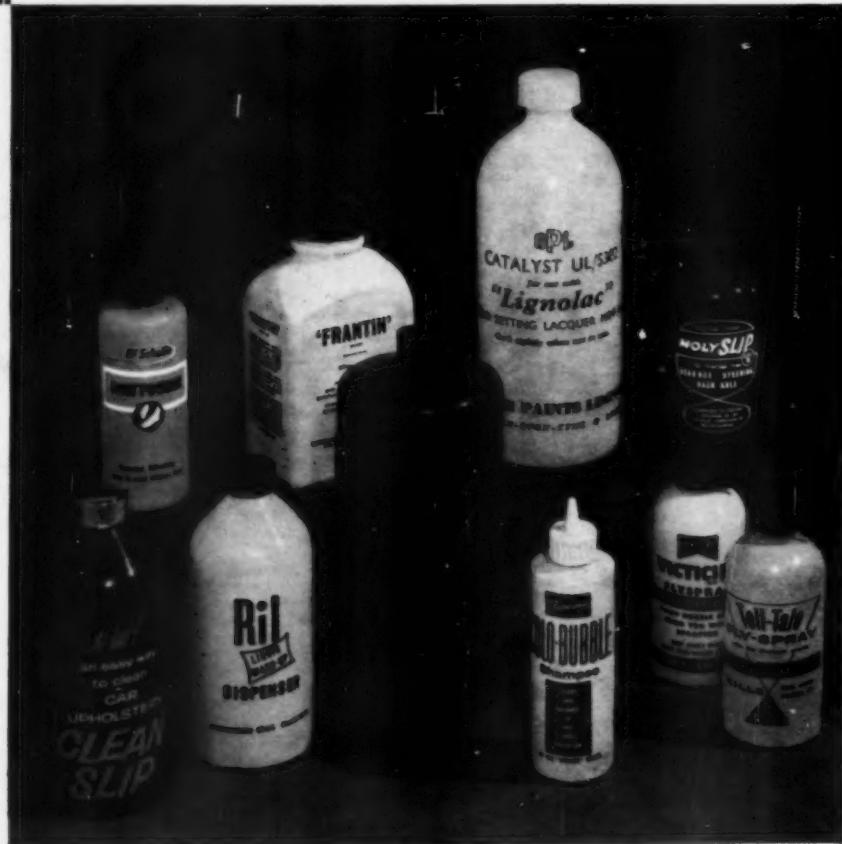


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